

=> fil reg; d stat que 19; fil cap1; d que nos 110; fil uspatf; d que nos 115  
FILE: 'REGISTRY' ENTERED AT 11:06:23 ON 20 MAR 2003  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 19 MAR 2003 HIGHEST RN 500101-42-8  
DICTIONARY FILE UPDATES: 19 MAR 2003 HIGHEST RN 500101-42-8

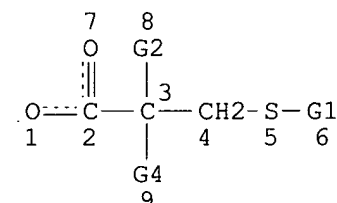
TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

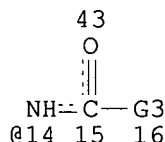
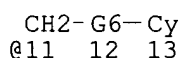
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

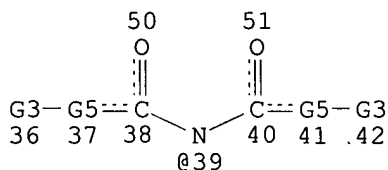
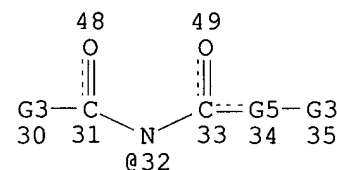
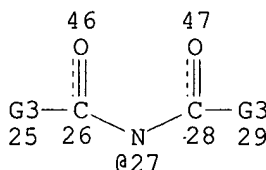
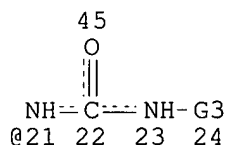
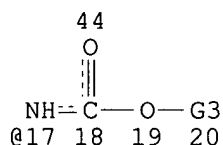
L1 STR



Ak @10



*full file  
search done  
on this structure*



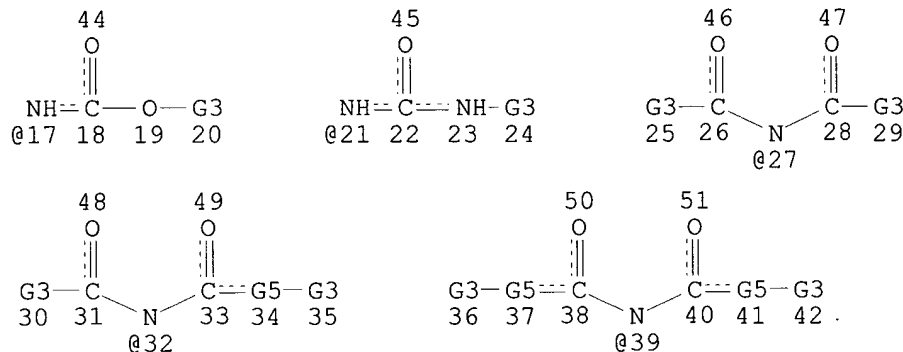
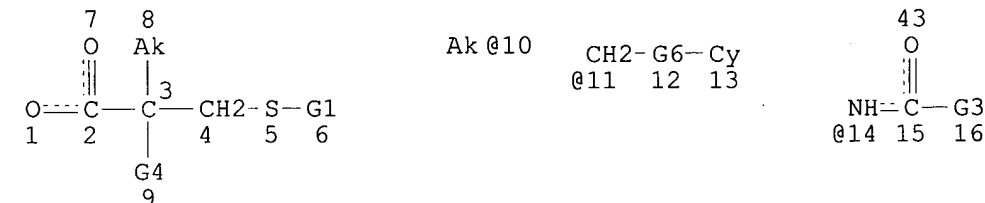
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VAR G2=C/CY/S/O/N  
VAR G3=H/CB/C  
VAR G4=OH/F/NH2/14/17/21/27/32/39  
VAR G5=O/NH  
REP G6=(0-5) CH2  
NODE ATTRIBUTES:  
CONNECT IS E1 RC AT 10  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 51

STEREO ATTRIBUTES: NONE

L2 380 SEA FILE=REGISTRY SSS FUL L1

L3 STR



VAR G1=10/CY/11

VAR G3=H/CB/C

VAR G4=NH<sub>2</sub>/14/17/21/27/32/39

VAR G5=O/NH

REP G6=(0-5) CH<sub>2</sub>

NODE ATTRIBUTES:

CONNECT IS E1 RC AT 8

CONNECT IS E1 RC AT 10

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

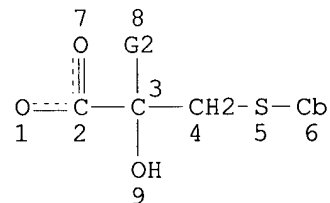
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NUMBER OF NODES IS 51

STEREO ATTRIBUTES: NONE

L4 STR



VAR G2=ME/ET

NODE ATTRIBUTES:

CONNECT IS M2 RC AT

DEFAULT MLEVEL IS ATOM

GGCAT IS MCY UNS AT 6

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS E6 C AT 6

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

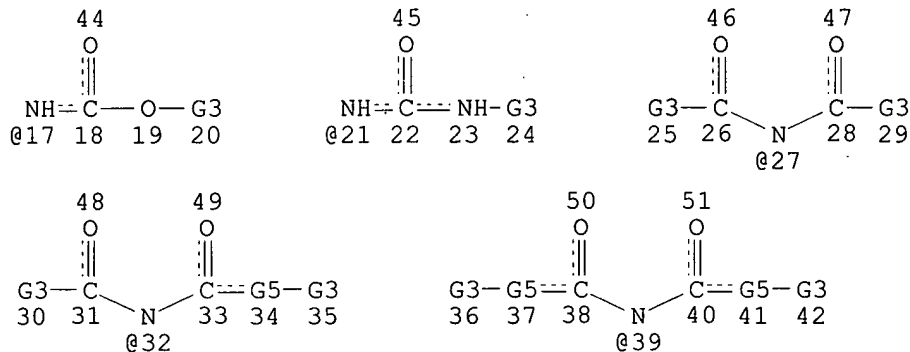
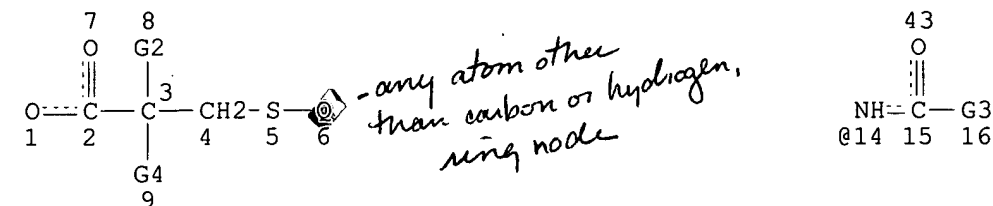
the following  
4 structures  
"NOT"-cd out of  
answer set to ~~mean~~  
meet provisos

6 - Carbocycle at node 6 has at least 1 substituent

NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE

L5 STR



VAR G2=C/CY/S/O/N

VAR G3=H/CB/C

VAR G4=OH/F/NH2/14/17/21/27/32/39

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NODE ATTRIBUTES:

NSPEC IS R AT 6

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

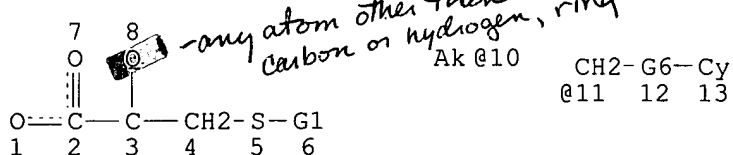
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NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE

L6 STR



VAR G1=10/CY/11

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NSPEC IS R AT 8

CONNECT IS E1 RC AT 10

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

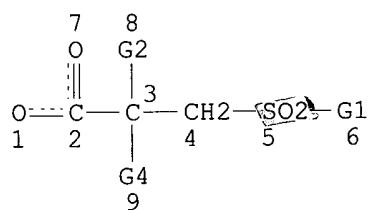
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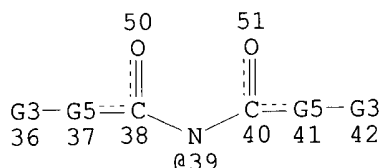
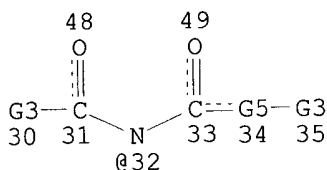
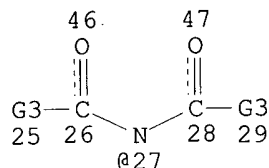
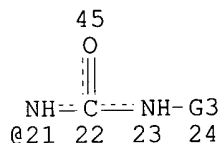
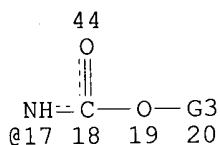
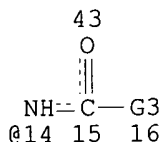
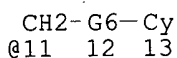
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

L7 STR



Ak @10



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 VAR G2=C/CY/S/O/N  
 VAR G3=H/CB/C  
 VAR G4=OH/F/NH2/14/17/21/27/32/39  
 VAR G5=O/NH  
 REP G6=(0-5) CH2  
 NODE ATTRIBUTES:  
 CONNECT IS E1 RC AT 10  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

*subset search  
done on this structure*

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 51

STEREO ATTRIBUTES: NONE  
~~L9~~ 106 SEA FILE=REGISTRY SUB=L2 SSS FUL (L7 NOT ((L3 OR L4 OR L5 OR L6)))

100.0% PROCESSED 141 ITERATIONS  
 SEARCH TIME: 00.00.01

106 ANSWERS

FILE 'CAPLUS' ENTERED AT 11:06:24 ON 20 MAR 2003  
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FILE COVERS 1907 - 20 Mar 2003 VOL 138 ISS 12  
FILE LAST UPDATED: 19 Mar 2003 (20030319/ED)

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

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L2          380 SEA FILE=REGISTRY SSS FUL L1
L3          STR
L4          STR
L5          STR
L6          STR
L7          STR
L9          106 SEA FILE=REGISTRY SUB=L2 SSS FUL (L7 NOT ((L3 OR L4 OR L5 OR
              L6)))
L10         6 SEA FILE=CAPLUS ABB=ON L9
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FILE 'USPATFULL' ENTERED AT 11:06:24 ON 20 MAR 2003  
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 Mar 2003 (20030318/PD)  
FILE LAST UPDATED: 18 Mar 2003 (20030318/ED)  
HIGHEST GRANTED PATENT NUMBER: US6536043  
HIGHEST APPLICATION PUBLICATION NUMBER: US2003051284  
CA INDEXING IS CURRENT THROUGH 18 Mar 2003 (20030318/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Mar 2003 (20030318/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2002  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2002

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>>> USPAT2 is now available.  USPATFULL contains full text of the    <<<
>>> original, i.e., the earliest published granted patents or        <<<
>>> applications.  USPAT2 contains full text of the latest US        <<<
>>> publications, starting in 2001, for the inventions covered in    <<<
>>> USPATFULL.  A USPATFULL record contains not only the original    <<<
>>> published document but also a list of any subsequent              <<<
>>> publications.  The publication number, patent kind code, and     <<<
>>> publication date for all the US publications for an invention    <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL  <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc.                                                         <<<
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>>> USPATFULL and USPAT2 can be accessed and searched together      <<<
>>> through the new cluster USPATALL.  Type FILE USPATALL to        <<<
>>> enter this cluster.                                              <<<
>>>                                                                    <<<
>>> Use USPATALL when searching terms such as patent assignees,      <<<
>>> classifications, or claims, that may potentially change from    <<<
>>> the earliest to the latest publication.                          <<<
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This file contains CAS Registry Numbers for easy and accurate  
substance identification.

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L1          STR
L2          380 SEA FILE=REGISTRY SSS FUL L1
L3          STR
L4          STR
L5          STR
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L6 STR  
L7 STR  
L9 106 SEA FILE=REGISTRY SUB=L2 SSS FUL (L7 NOT ((L3 OR L4 OR L5 OR  
L6)))  
L15 1 SEA FILE=USPATFULL ABB=ON L9

=> dup rem 110,115

FILE 'CAPLUS' ENTERED AT 11:06:30 ON 20 MAR 2003

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PROCESSING COMPLETED FOR L10

PROCESSING COMPLETED FOR L15

L17 7 DUP REM L10 L15 (0 DUPLICATES REMOVED)

ANSWERS '1-6' FROM FILE CAPLUS

ANSWER '7' FROM FILE USPATFULL

=> d ibib abs hitstr 1-7; fil cao; d que nos 116

~~L17~~ ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:72030 CAPLUS

DOCUMENT NUMBER: 136:134761

TITLE: Preparation of 3-arylsulfonyl-2-hydroxy-2-methylpropanoic acids as inhibitors of matrix metallo-proteinases (MMPs)

INVENTOR(S): Mantegani, Sergio; Bissolino, Pierluigi; Abrate, Francesca; Cremonesi, Paolo; Perrone, Ettore

PATENT ASSIGNEE(S): Pharmacia & Upjohn S.p.A., Italy

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

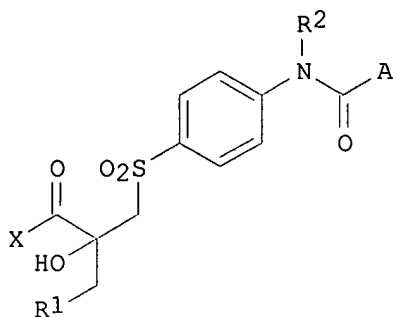
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006215	A1	20020124	WO 2001-EP7736	20010705
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: GB 2000-17435 A 20000714

OTHER SOURCE(S): MARPAT 136:134761

GI



I

AB The title compds. [I; X = NHOH, OH; R1 = OPh, SPh, SHet, Hyd, CH2Hyd; Het = heterocyclic ring; Hyd = substituted hydantoin-3-yl ring; A = Ph, Het, condensed Ph ring; R2 = H, Me; or R2 represents a methylene bridge connecting the N atom to the ortho position of said A to form a 5-membered lactam] or their salts which are inhibitors of matrix metallo-proteinases (MMPs) and are therefore useful in the prevention, control and treatment of diseases in which MMPs are involved, were prepd. E.g., a multi-step synthesis of I [A = 4-ClC6H4; X = OH; R1 = (3,4,4-trimethylhydantoin-1-yl)CH2; R2 = H] which showed Ki of 14.7 nM against MMP-2, was given.

IT 391903-52-9P 391903-53-0P 391903-54-1P  
 391903-55-2P 391903-56-3P 391903-57-4P  
 391903-58-5P 391903-59-6P 391903-60-9P  
 391903-61-0P 391903-62-1P 391903-63-2P  
 391903-64-3P 391903-65-4P 391903-66-5P  
 391903-67-6P 391903-68-7P 391903-69-8P  
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 391903-73-4P 391903-74-5P 391903-76-7P  
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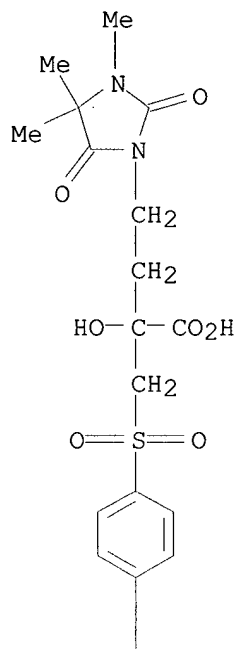
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3-arylsulfonyl-2-hydroxy-2-methylpropanoic acids as inhibitors of matrix metallo-proteinases (MMPs))

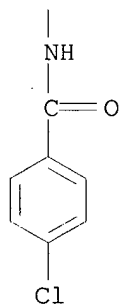
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CN 1-Imidazolidinebutanoic acid, .alpha.-[[[4-[(4-chlorobenzoyl)amino]phenyl]sulfonyl]methyl]-.alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo- (9CI) (CA INDEX NAME)

PAGE 1-A



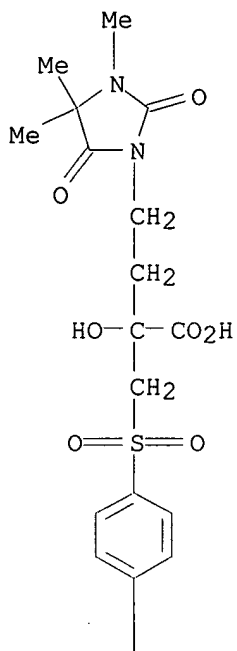
PAGE 2-A



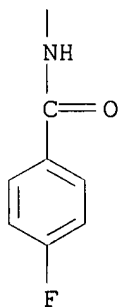
RN 391903-53-0 CAPLUS  
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PAGE 1-A

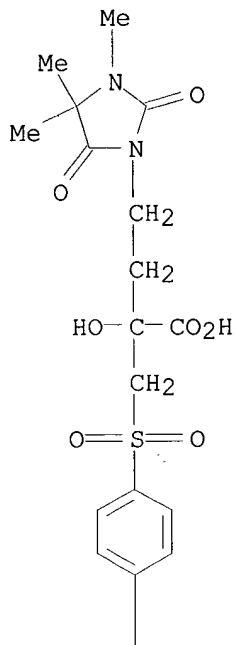


PAGE 2-A

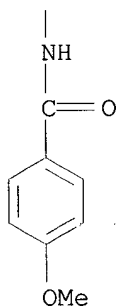


RN 391903-54-1 CAPLUS  
CN 1-Imidazolidinebutanoic acid, .alpha.-hydroxy-.alpha.-[[[4-[(4-methoxybenzoyl)amino]phenyl]sulfonyl]methyl]-3,4,4-trimethyl-2,5-dioxo-(9CI) (CA INDEX NAME)

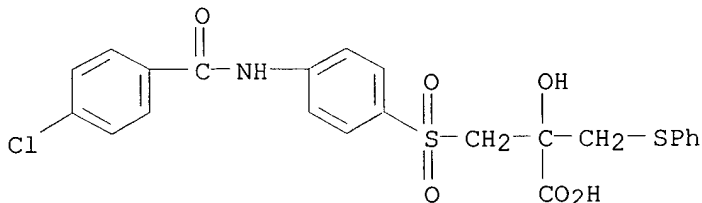
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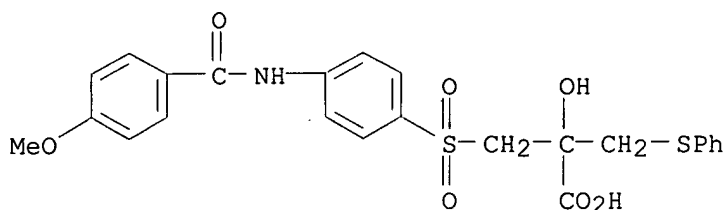
PAGE 2-A



RN 391903-55-2 CAPLUS  
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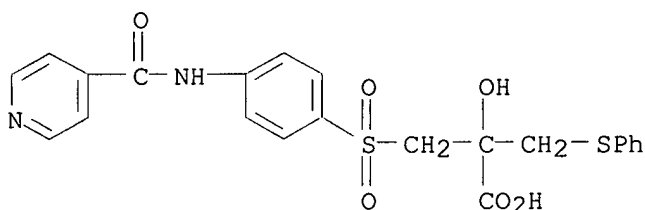


RN 391903-56-3 CAPLUS  
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 methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



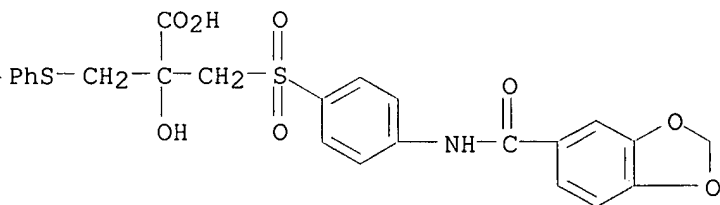
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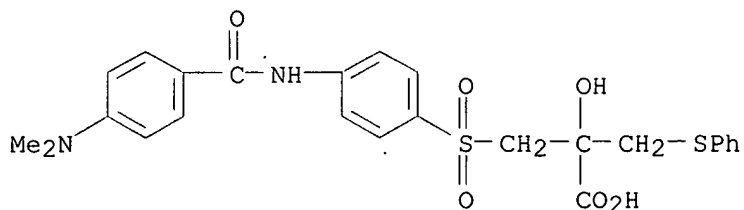
RN 391903-58-5 CAPLUS

CN Propanoic acid, 3-[[4-[(1,3-benzodioxol-5-ylcarbonyl)amino]phenyl]sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]- (9CI) (CA INDEX NAME)



RN 391903-59-6 CAPLUS

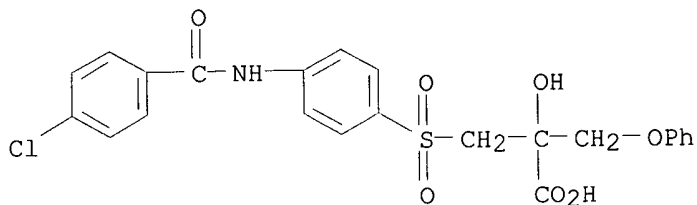
CN Propanoic acid, 3-[[4-[[4-(dimethylamino)benzoyl]amino]phenyl]sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]-, monosodium salt (9CI) (CA INDEX NAME)



Na

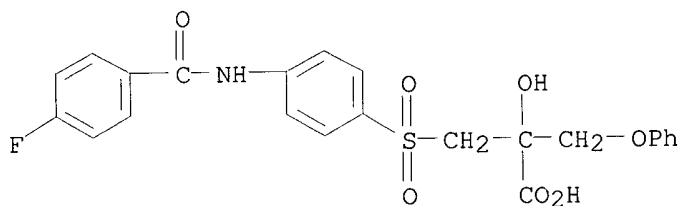
RN 391903-60-9 CAPLUS

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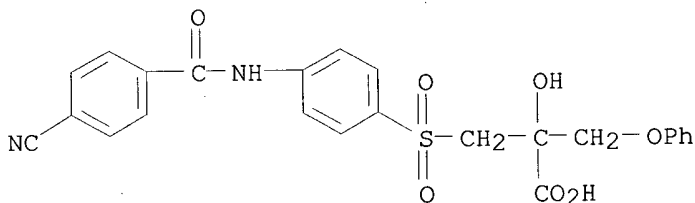
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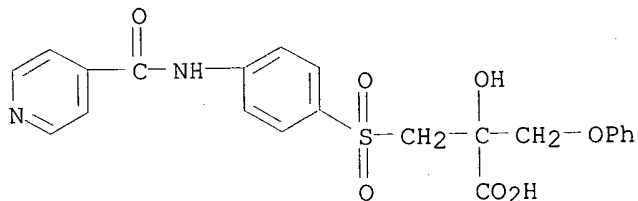
RN 391903-62-1 CAPLUS

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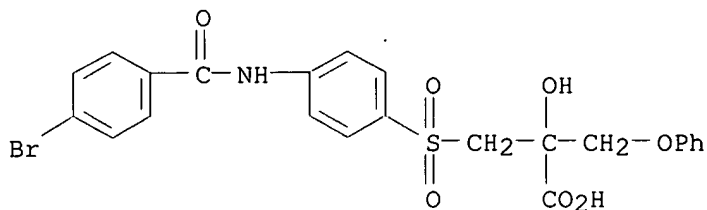
RN 391903-63-2 CAPLUS

CN Propanoic acid, 2-hydroxy-2-(phenoxy)methyl)-3-[[4-[(4-pyridinylcarbonyl)amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



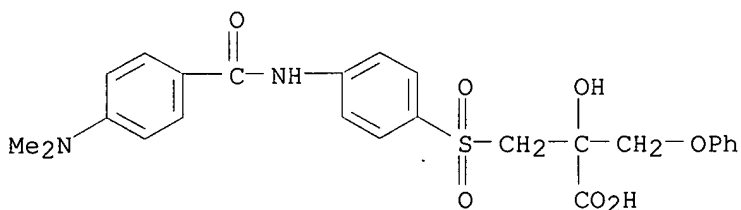
RN 391903-64-3 CAPLUS

CN Propanoic acid, 3-[[4-[(4-bromobenzoyl)amino]phenyl]sulfonyl]-2-hydroxy-2-(phenoxy)methyl)- (9CI) (CA INDEX NAME)



RN 391903-65-4 CAPLUS

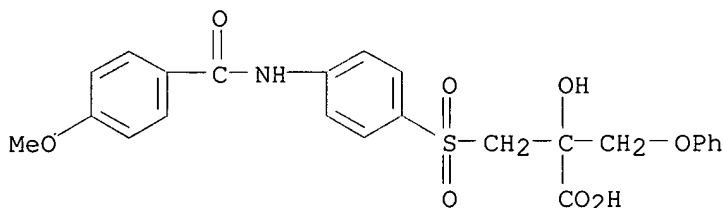
CN Propanoic acid, 3-[[4-[[4-(dimethylamino)benzoyl]amino]phenyl]sulfonyl]-2-hydroxy-2-(phoxymethyl)-, monosodium salt (9CI) (CA INDEX NAME)



● Na

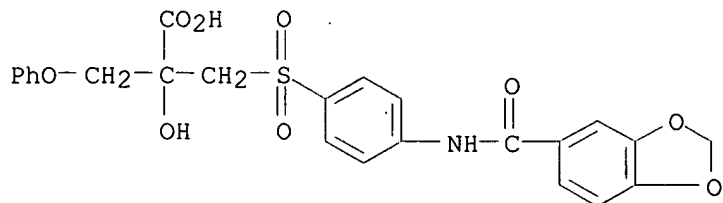
RN 391903-66-5 CAPLUS

CN Propanoic acid, 2-hydroxy-2-[[[4-[(4-methoxybenzoyl)amino]phenyl]sulfonyl]methyl]-3-phenoxy- (9CI) (CA INDEX NAME)



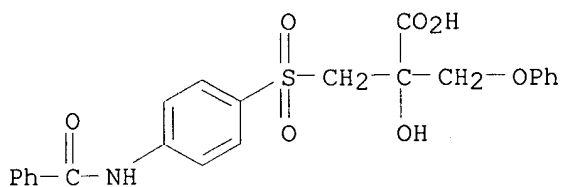
RN 391903-67-6 CAPLUS

CN Propanoic acid, 3-[[4-[(1,3-benzodioxol-5-ylcarbonyl)amino]phenyl]sulfonyl]-2-hydroxy-2-(phoxymethyl)- (9CI) (CA INDEX NAME)



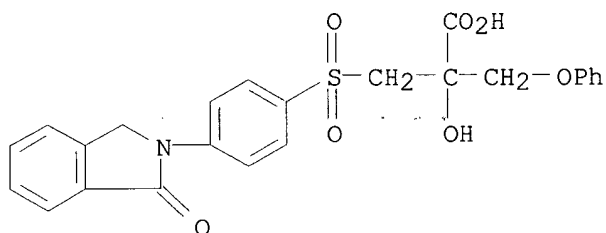
RN 391903-68-7 CAPLUS

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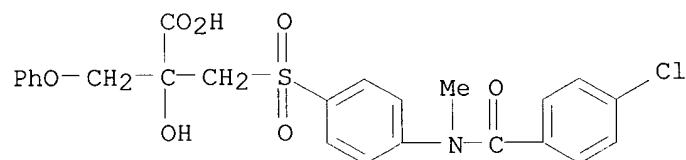
RN 391903-69-8 CAPLUS

CN Propanoic acid, 3-[[4-[(1,3-dihydro-1-oxo-2H-isoindol-2-yl)phenyl]sulfonyl]-2-hydroxy-2-(phenoxy)methyl]- (9CI) (CA INDEX NAME).



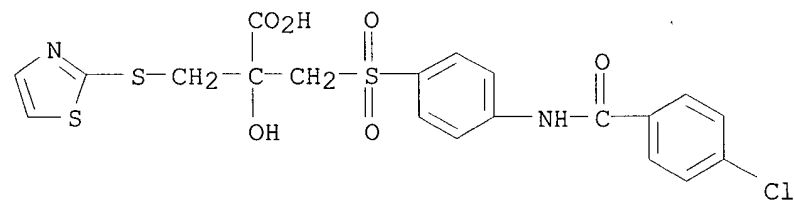
RN 391903-70-1 CAPLUS

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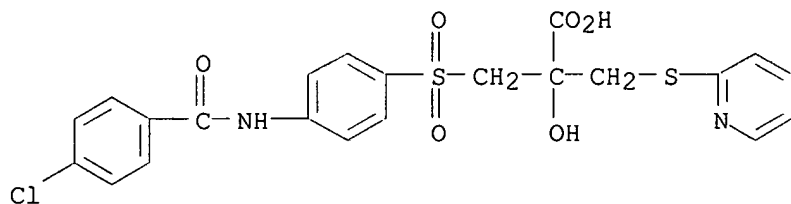
RN 391903-71-2 CAPLUS

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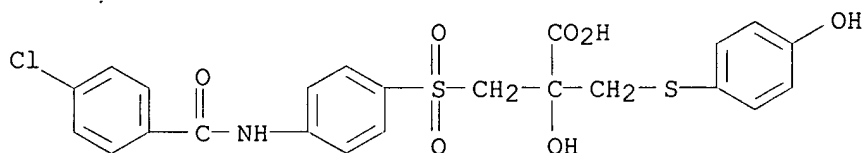
RN 391903-72-3 CAPLUS

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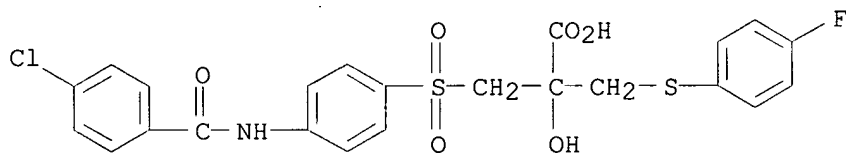
RN 391903-73-4 CAPLUS

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RN 391903-74-5 CAPLUS

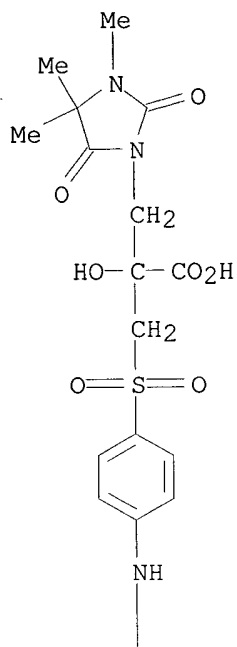
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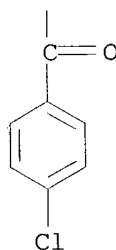
RN 391903-76-7 CAPLUS

CN 1-Imidazolidinepropanoic acid, .alpha.-[[[4-[(4-chlorobenzoyl)amino]phenyl]sulfonyl]methyl]-.alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo- (9CI) (CA INDEX NAME)

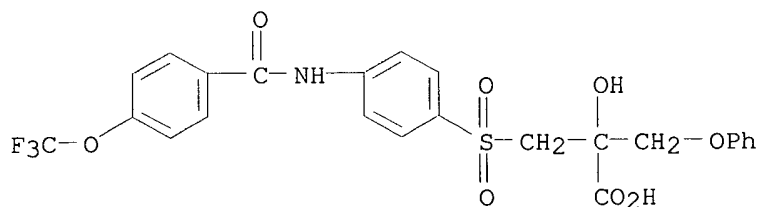
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PAGE 2-A

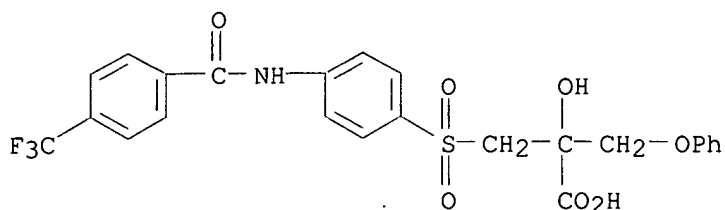


RN 391903-77-8 CAPLUS  
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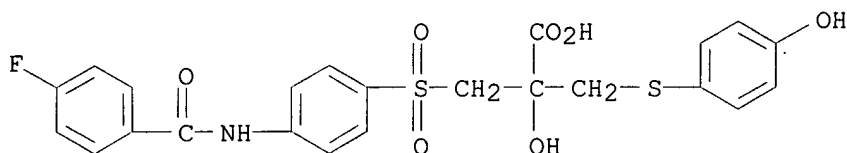
RN 391903-78-9 CAPLUS  
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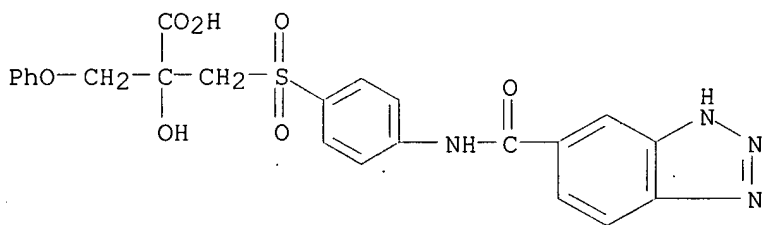
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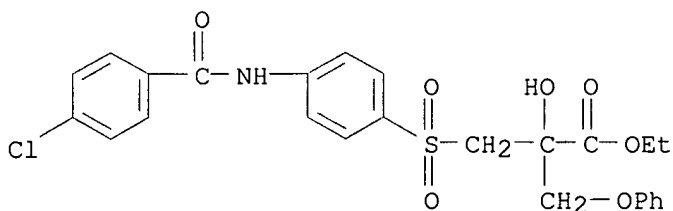
RN 391904-13-5 CAPLUS

CN Propanoic acid, 3-[[4-[(1H-benzotriazol-5-ylcarbonyl)amino]phenyl]sulfonyl]-2-hydroxy-2-(phenoxymethyl)- (9CI) (CA INDEX NAME)



RN 391904-14-6 CAPLUS

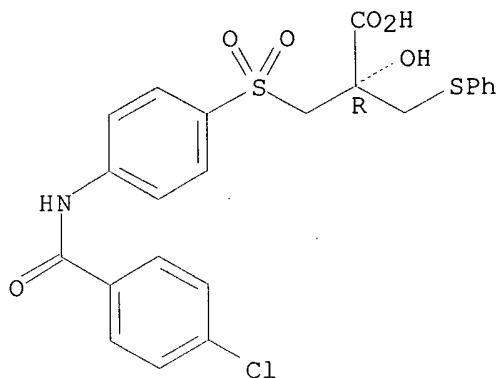
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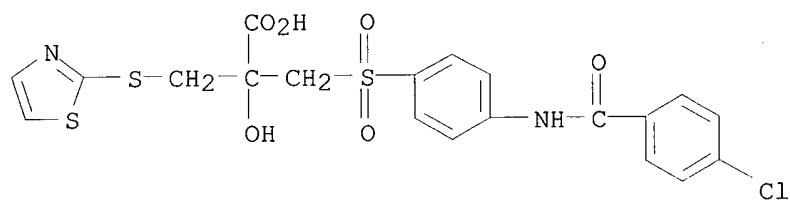
RN 391904-15-7 CAPLUS

CN Propanoic acid, 3-[[4-[(4-chlorobenzoyl)amino]phenyl]sulfonyl]-2-hydroxy-2-phenylthiomethyl]- (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

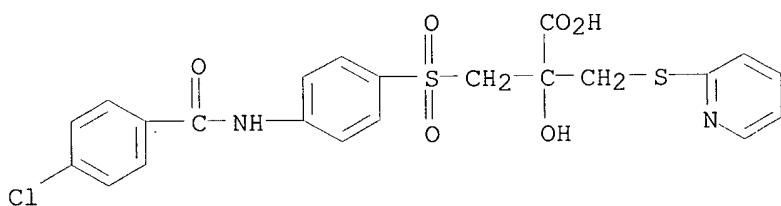


RN 391904-16-8 CAPLUS  
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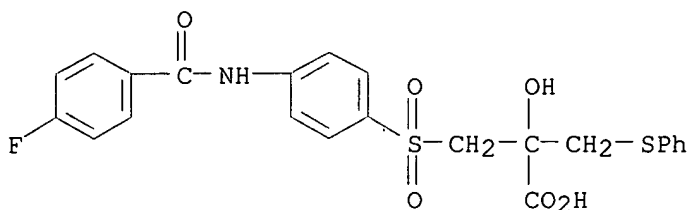
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RN 391904-18-0 CAPLUS  
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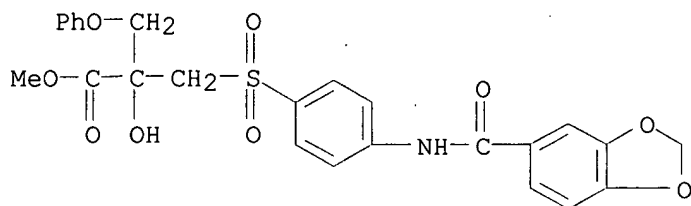
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RN 391904-19-1 CAPLUS  
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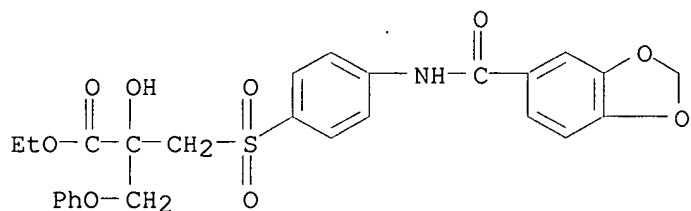
RN 391904-20-4 CAPLUS

CN Propanoic acid, 3-[[4-[(1,3-benzodioxol-5-ylcarbonyl)amino]phenyl]sulfonyl]-2-hydroxy-2-(phenoxymethyl)-, methyl ester (9CI) (CA INDEX NAME)



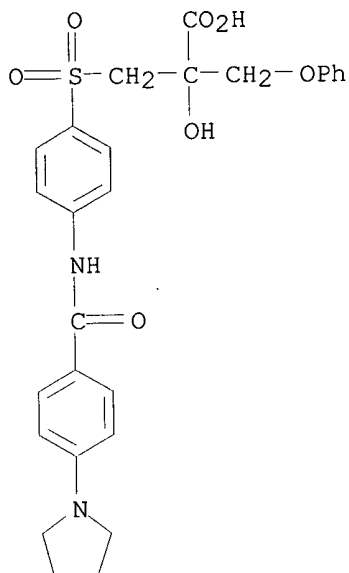
RN 391904-21-5 CAPLUS

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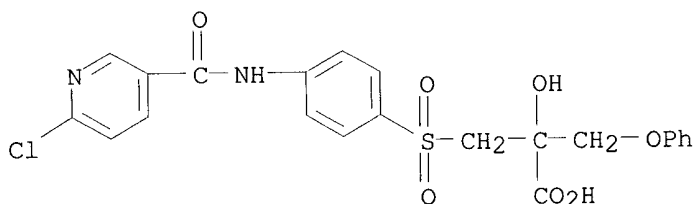


RN 391904-22-6 CAPLUS

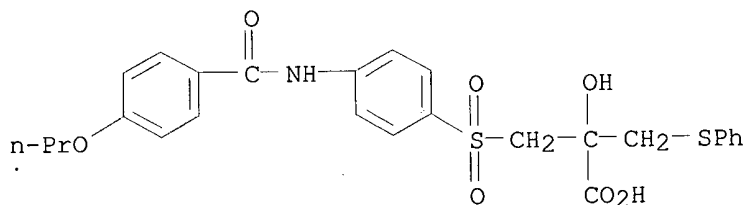
CN Propanoic acid, 2-hydroxy-2-(phenoxymethyl)-3-[[4-[[4-(1-pyrrolidinyl)benzoyl]amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



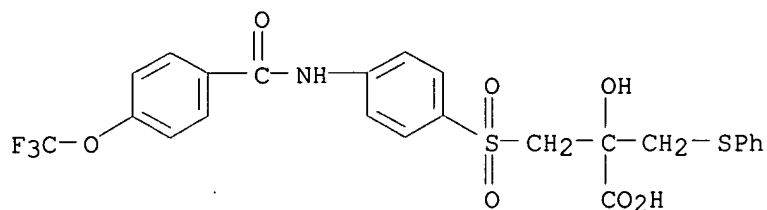
RN 391904-23-7 CAPLUS  
 CN Propanoic acid, 3-[[4-[[[(6-chloro-3-pyridinyl)carbonyl]amino]phenyl]sulfonyl]-2-hydroxy-2-(phenoxymethyl)- (9CI) (CA INDEX NAME)



RN 391904-24-8 CAPLUS  
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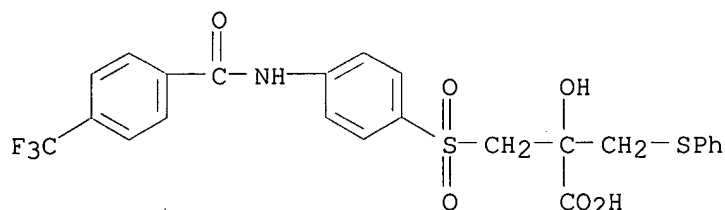


RN 391904-25-9 CAPLUS  
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RN 391904-26-0 CAPLUS

CN Propanoic acid, 2-hydroxy-2-[(phenylthio)methyl]-3-[[4-[[4-(trifluoromethyl)benzoyl]amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

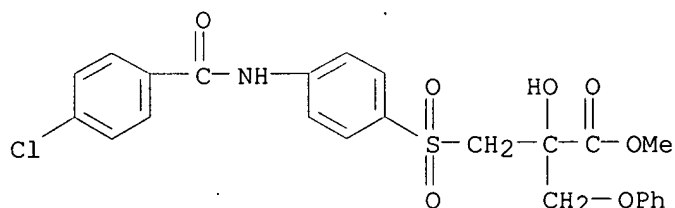


IT 391904-12-4

RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of 3-arylsulfonyl-2-hydroxy-2-methylpropanoic acids as  
inhibitors of matrix metallo-proteinases (MMPs))

RN 391904-12-4 CAPLUS

CN Propanoic acid, 3-[[4-[[4-(4-chlorobenzoyl)amino]phenyl]sulfonyl]-2-hydroxy-2-(phenoxy)methyl]-, methyl ester (9CI) (CA INDEX NAME)



IT 391903-84-7P 391903-85-8P 391903-86-9P  
391903-90-5P 391903-91-6P 391903-92-7P  
391903-93-8P 391903-94-9P 391903-95-0P  
391903-96-1P 391903-97-2P 391903-98-3P  
391903-99-4P 391904-00-0P 391904-01-1P  
391904-07-7P

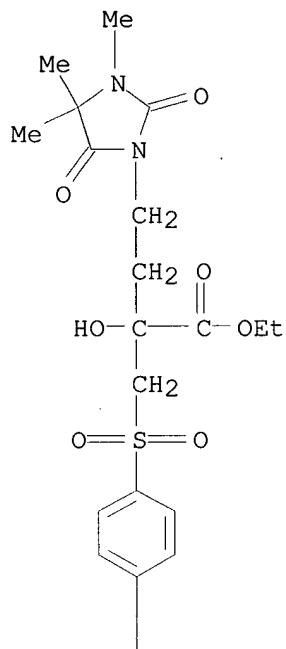
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(prepn. of 3-arylsulfonyl-2-hydroxy-2-methylpropanoic acids as  
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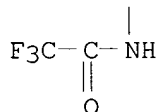
RN 391903-84-7 CAPLUS

CN 1-Imidazolidinebutanoic acid, .alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-  
.alpha.-[[[4-[(trifluoroacetyl)amino]phenyl]sulfonyl]methyl]-, ethyl ester  
(9CI) (CA INDEX NAME)

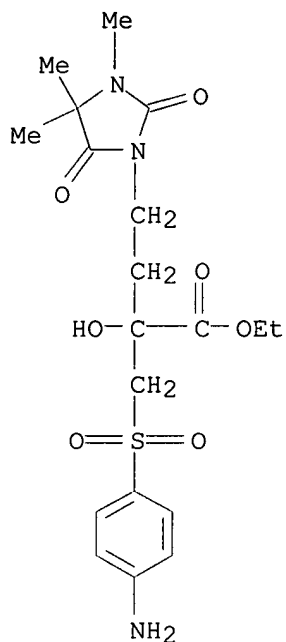
PAGE 1-A



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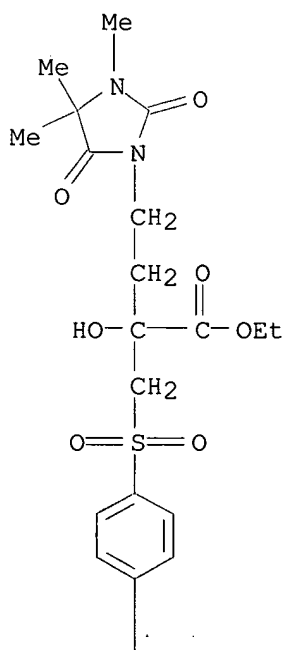


RN 391903-85-8 CAPLUS  
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.alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-, ethyl ester (9CI) (CA INDEX  
NAME)

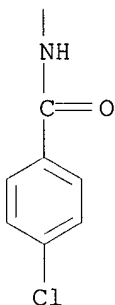


RN 391903-86-9 CAPLUS  
CN 1-Imidazolidinebutanoic acid, .alpha.-[[[4-[(4-chlorobenzoyl)amino]phenyl]sulfonyl]methyl]-.alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

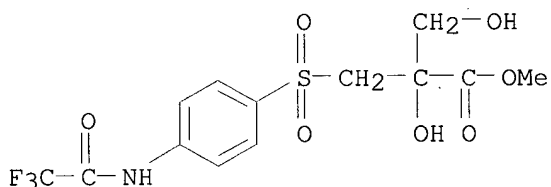
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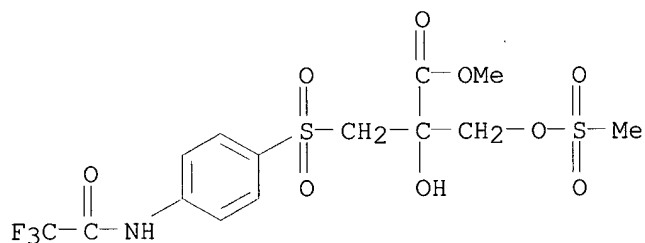
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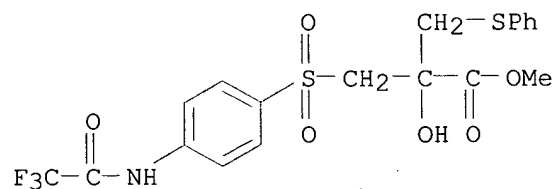
RN 391903-90-5 CAPLUS  
 CN Propanoic acid, 2,3-dihydroxy-2-[[[4-[(trifluoroacetyl)amino]phenyl]sulfonyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 391903-91-6 CAPLUS  
 CN Propanoic acid, 2-hydroxy-2-[[[4-[(trifluoroacetyl)amino]phenyl]sulfonyl]methyl]-3-[[4-[(trifluoroacetyl)amino]phenyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)



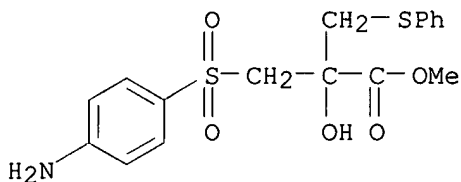
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RN 391903-93-8 CAPLUS  
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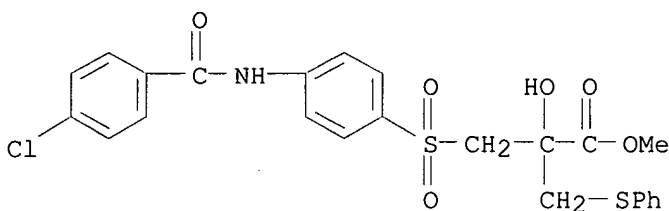


[(phenylthio)methyl]-, methyl ester (9CI) (CA INDEX NAME)



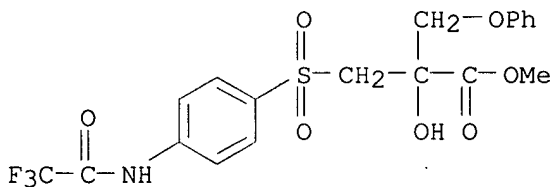
RN 391903-94-9 CAPLUS

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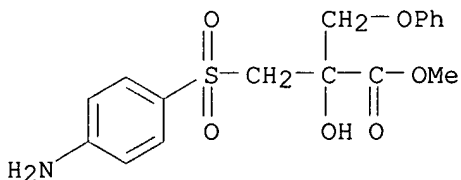
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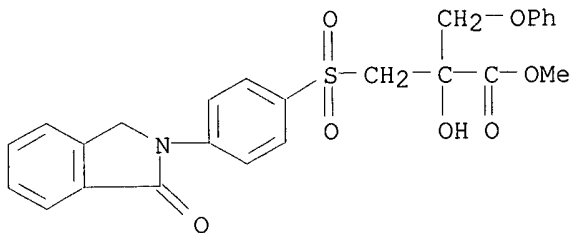
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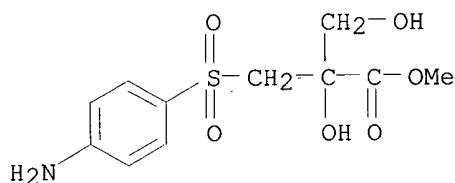
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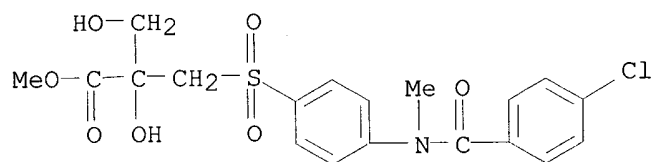
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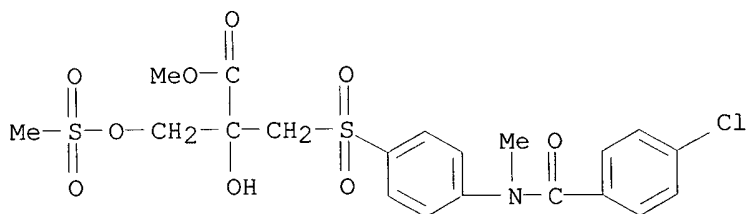
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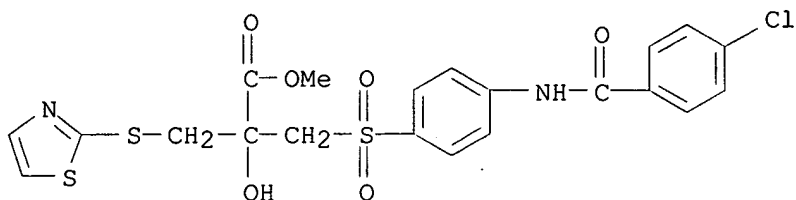
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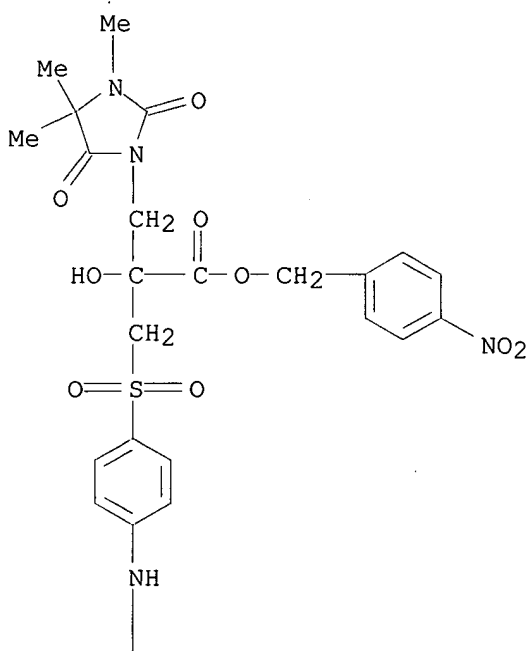
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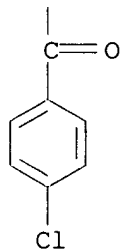


RN 391904-07-7 CAPLUS  
CN 1-Imidazolidinepropanoic acid, .alpha.-[[[4-[(4-chlorobenzoyl)amino]phenyl]sulfonyl]methyl]-.alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

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REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2001:396841 CAPLUS

Searched by Barb O'Bryen, STIC 308-4291

DOCUMENT NUMBER: 135:5449  
TITLE: Preparation of (R)-3-(4-chlorobiphenylsulfonyl)-2-hydroxy-2-(phenylthio)methylpropionic acid and its use as a matrix metalloproteinase inhibitor in the treatment of cancer  
INVENTOR(S): Bissolino, Pierluigi; Mantegani, Sergio; Orzi, Fabrizio; Jabes, Daniela; Alzani, Rachele; D'anello, Matteo; Perrone, Ettore  
PATENT ASSIGNEE(S): Pharmacia & Upjohn S.P.A., Italy  
SOURCE: PCT Int. Appl., 25 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038301	A1	20010531	WO 2000-EP10837	20001101

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-27453 A 19991119

OTHER SOURCE(S): CASREACT 135:5449

AB (R)-3-(4-chlorobiphenylsulfonyl)-2-hydroxy-2-(phenylthio)methylpropionic acid and its salts, useful as a matrix metalloproteinase inhibitor in the treatment of cancers, is prepd. along with its salts.

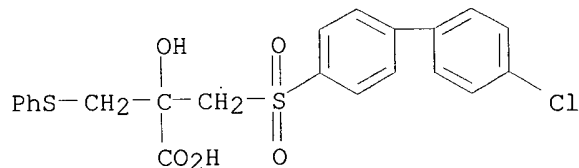
IT **226419-98-3P 341498-80-4P 341498-84-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in the prepn. of (R)-3-(4-chlorobiphenylsulfonyl)-2-hydroxy-2-(phenylthio)methylpropionic acid and its salts as matrix metalloproteinase inhibitors useful in the treatment of cancers)

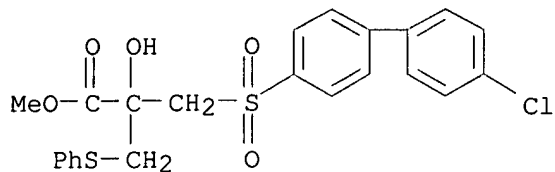
RN 226419-98-3 CAPLUS

CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]- (9CI) (CA INDEX NAME)



RN 341498-80-4 CAPLUS

CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 341498-84-8 CAPLUS

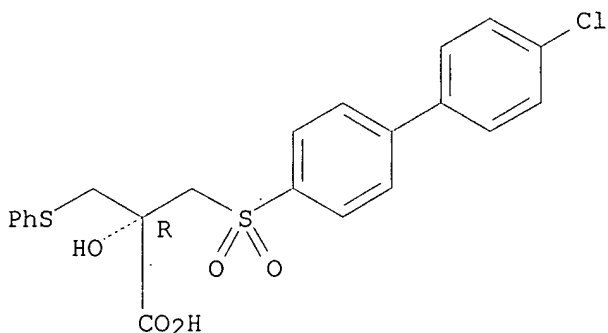
CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]-, (2R)-, compd. with (.alpha.S)-.alpha.-[(1R)-1-(methylamino)ethyl]benzenemethanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 341498-83-7

CMF C22 H19 Cl O5 S2

Absolute stereochemistry. Rotation (+).

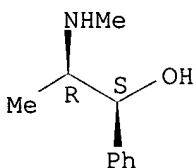


CM 2

CRN 321-98-2

CMF C10 H15 N O

Absolute stereochemistry. Rotation (+).



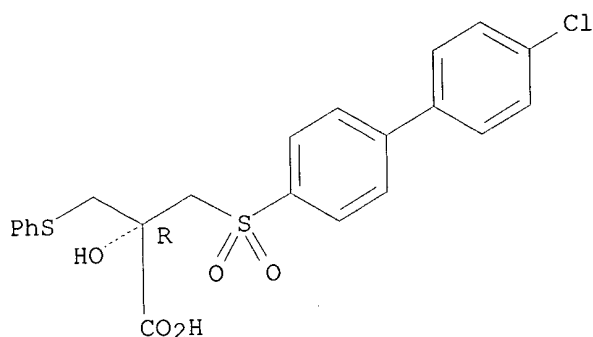
IT 341498-83-7P 341498-89-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(prepn. of (R)-3-(4-chlorobiphenylsulfonyl)-2-hydroxy-2-[(phenylthio)methyl]propanoic acid and its salts as matrix metalloproteinase inhibitors useful in the treatment of cancers)

RN 341498-83-7 CAPLUS

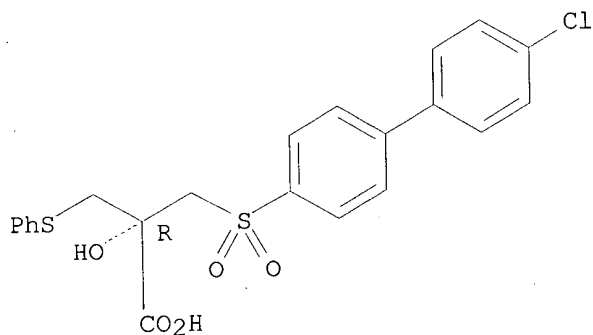
CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 341498-89-3 CAPLUS  
 CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]-, monosodium salt, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● Na

IT 341498-92-8P 341498-95-1P 341498-98-4P  
 341499-01-2P 341499-04-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of (R)-3-(4-chlorobiphenylsulfonyl)-2-hydroxy-2-[(phenylthio)methyl]propionic acid and its salts as matrix metalloproteinase inhibitors useful in the treatment of cancers)

RN 341498-92-8 CAPLUS

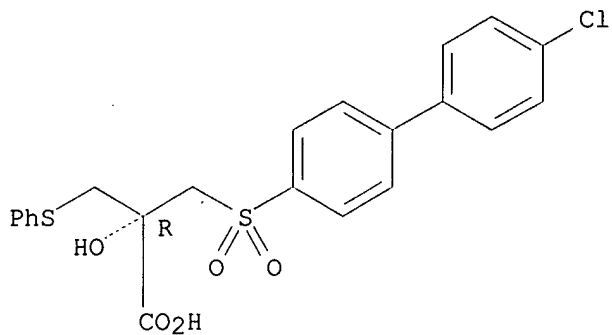
CN L-Arginine, mono[(2R)-3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]propanoate] (9CI) (CA INDEX NAME)

CM 1

CRN 341498-83-7

CMF C22 H19 Cl O5 S2

Absolute stereochemistry. Rotation (+).

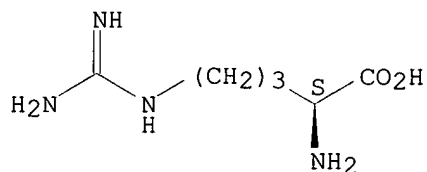


CM 2

CRN 74-79-3

CMF C6 H14 N4 O2

Absolute stereochemistry.



RN 341498-95-1 CAPLUS

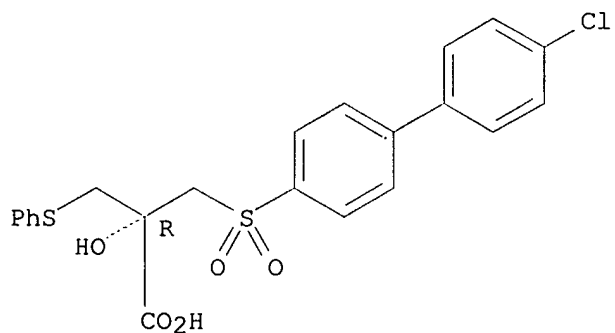
CN D-Glucitol, 1-deoxy-1-(methylamino)-, (2R)-3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]propanoate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 341498-83-7

CMF C22 H19 Cl O5 S2

Absolute stereochemistry. Rotation (+).

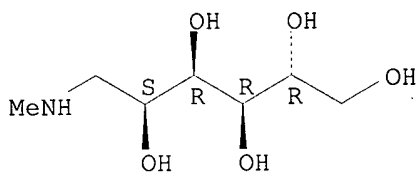


CM 2

CRN 6284-40-8

CMF C7 H17 N O5

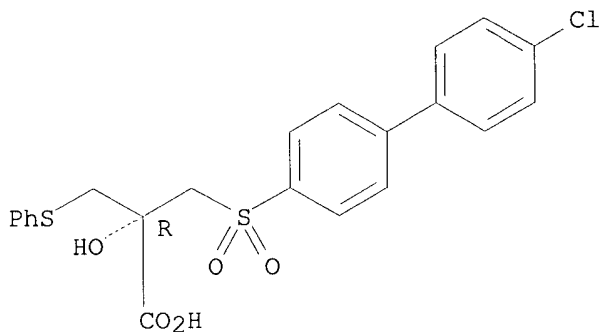
Absolute stereochemistry.



RN 341498-98-4 CAPLUS

CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]-, monopotassium salt, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

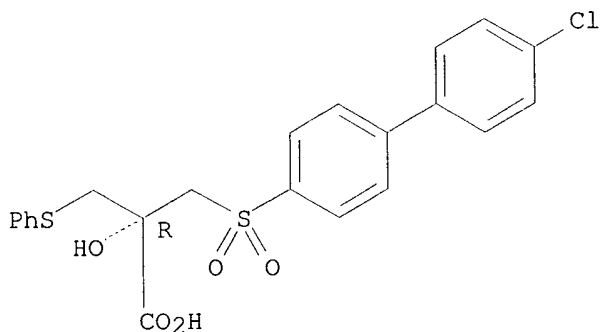


● K

RN 341499-01-2 CAPLUS

CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]-, calcium salt (2:1), (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



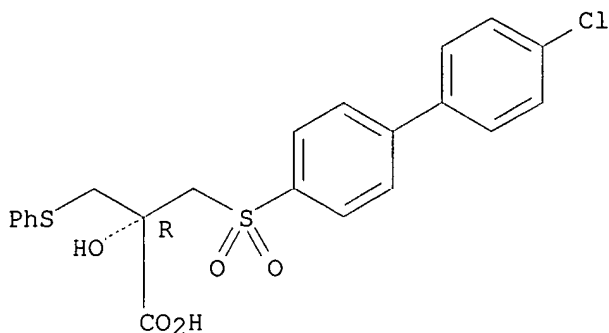
● 1/2 Ca

RN 341499-04-5 CAPLUS

CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(phenylthio)methyl]-, magnesium salt (2:1), (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





● 1/2 Mg

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:354468 CAPLUS

DOCUMENT NUMBER: 131:18833

TITLE: Preparation of .alpha.-hydroxy, -amino, and halo derivatives of .beta.-sulfonyl hydroxamic acids as matrix metalloproteinases inhibitors

INVENTOR(S): Warpehoski, Martha A.; Mitchell, Mark Allen; Harper, Donald E.; Maggiora, Linda Louise

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

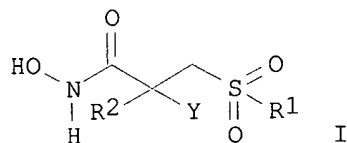
PATENT INFORMATION:

*Applicant*

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926909	A2	19990603	WO 1998-IB2154	19981118
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RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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EP 1037868	A2	20000927	EP 1998-966869	19981118
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R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
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JP 2001524462	T2	20011204	JP 2000-522069	19981118
AT 232192	E	20030215	AT 1998-966869	19981118
US 6437177	B1	20020820	US 1998-196190	19981120
NO 2000002505	A	20000630	NO 2000-2505	20000515
PRIORITY APPLN. INFO.:			US 1997-72655P	P 19971121
			WO 1998-IB2154	W 19981118

OTHER SOURCE(S):  
GI

MARPAT 131:18833



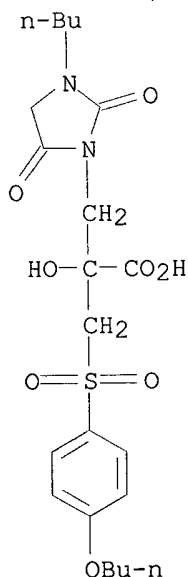
AB The title compds. [I; R1 = C4-12 alkyl, C4-12 alkenyl, C4-12 alkynyl, etc.; R2 = C1-12 alkyl, C4-12 alkenyl, C4-12 alkynyl, etc.; Y = OH, NR9R10, F; R9, R10 = H, COR3, CO2R3, etc.; R3 = H, cycloalkyl, alkyl, etc.], inhibitors of matrix metalloproteinases which are useful in treating osteoarthritis, rheumatoid arthritis, septic arthritis, osteoporosis, tumor metastasis, periodontitis, gingivitis, corneal ulceration, dermal ulceration, gastric ulceration, inflammation, or asthma, were prepd. E.g., a 7-step synthesis of I [R1 = 4-PhC6H4; R2 = 4-MeOC6H4SO2CH2; Y = OH] which showed Ki of 0.074 .mu.M and 0.0019 .mu.M against stromelysin and gelatinase, resp.

IT 226419-90-5P 226419-91-6P 226419-92-7P  
226419-93-8P 226419-94-9P 226419-95-0P  
226419-96-1P 226419-97-2P 226419-98-3P  
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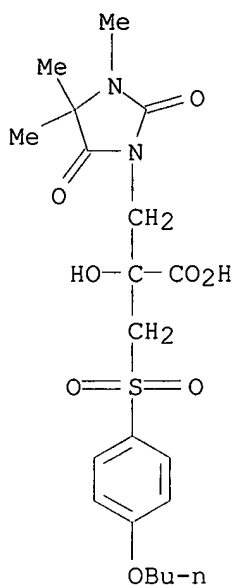
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of .alpha.-hydroxy, -amino, and halo derivs. of .beta.-sulfonyl hydroxamic acids as matrix metalloproteinases inhibitors)

RN 226419-90-5 CAPLUS

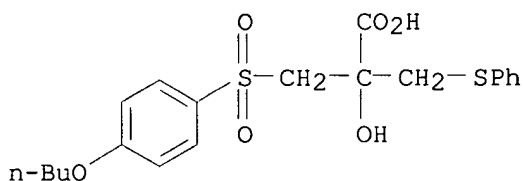
CN 1-Imidazolidinepropanoic acid, .alpha.-[[ (4-butoxyphenyl)sulfonyl]methyl]-3-butyl-.alpha.-hydroxy-2,5-dioxo- (9CI) (CA INDEX NAME)



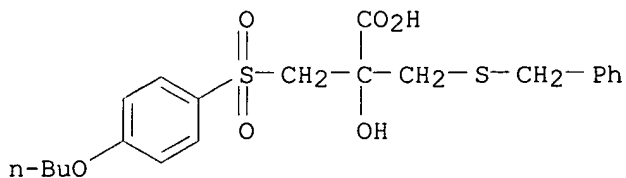
RN 226419-91-6 CAPLUS

CN 1-Imidazolidinepropanoic acid, .alpha.-[[ (4-butoxyphenyl)sulfonyl]methyl]-  
.alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo- (9CI) (CA INDEX NAME)

RN 226419-92-7 CAPLUS

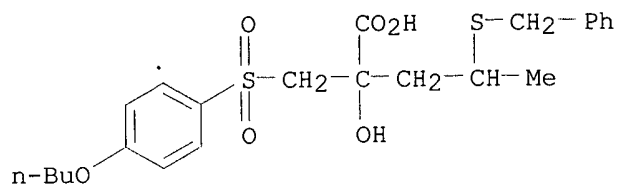
CN Propanoic acid, 3-[[ (4-butoxyphenyl)sulfonyl]-2-hydroxy-2-  
[(phenylthio)methyl]- (9CI) (CA INDEX NAME)

RN 226419-93-8 CAPLUS

CN Propanoic acid, 3-[[ (4-butoxyphenyl)sulfonyl]-2-hydroxy-2-  
[[ (phenylmethyl)thio]methyl]- (9CI) (CA INDEX NAME)

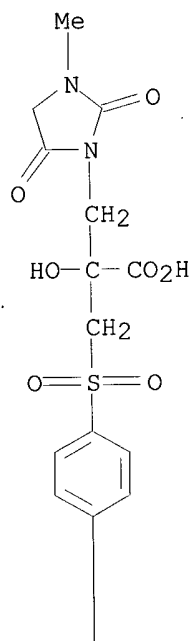
RN 226419-94-9 CAPLUS

CN Pentonic acid, 2-C-[[ (4-butoxyphenyl)sulfonyl]methyl]-3,5-dideoxy-4-S-  
(phenylmethyl)-4-thio- (9CI) (CA INDEX NAME)

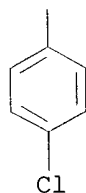


RN 226419-95-0 CAPLUS  
 CN 1-Imidazolidinepropanoic acid, .alpha.-[[[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]methyl]-.alpha.-hydroxy-3-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)

PAGE 1-A

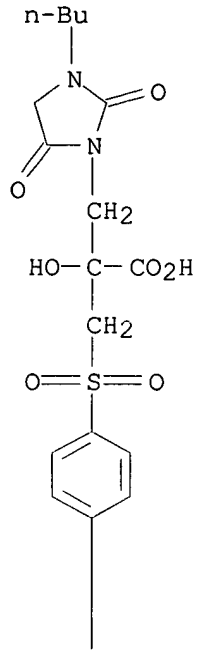


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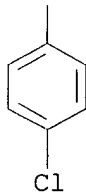


RN 226419-96-1 CAPLUS  
 CN 1-Imidazolidinepropanoic acid, 3-butyl-.alpha.-[[[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]methyl]-.alpha.-hydroxy-2,5-dioxo- (9CI) (CA INDEX NAME)

PAGE 1-A

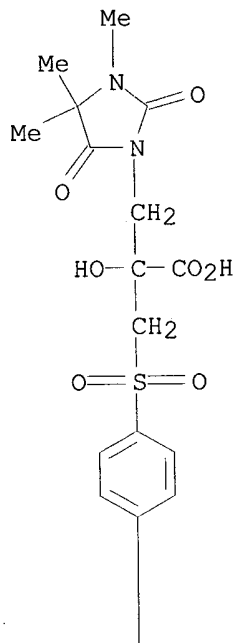


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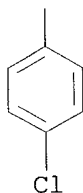


RN 226419-97-2 CAPLUS  
CN 1-Imidazolidinepropanoic acid, .alpha.-[[ (4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]methyl]-.alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo- (9CI) (CA INDEX NAME)

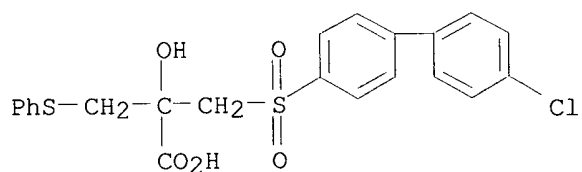
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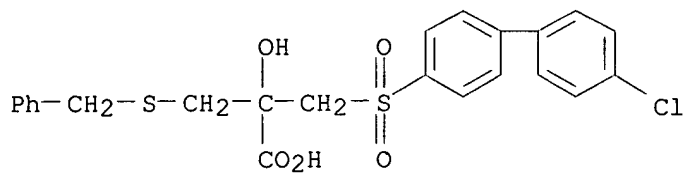
PAGE 2-A



RN 226419-98-3 CAPLUS  
 CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-  
 [(phenylthio)methyl]- (9CI) (CA INDEX NAME)

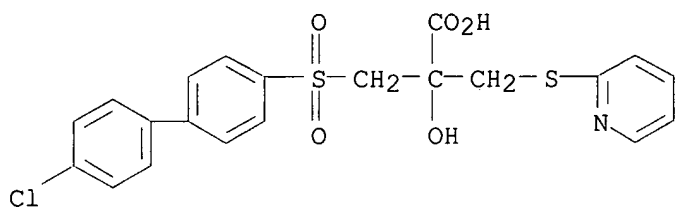


RN 226419-99-4 CAPLUS  
 CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-  
 [[(phenylmethyl)thio]methyl]- (9CI) (CA INDEX NAME)



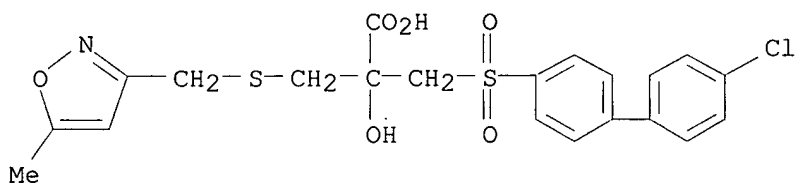
RN 226420-00-4 CAPLUS

CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(2-pyridinylthio)methyl]- (9CI) (CA INDEX NAME)



RN 226420-01-5 CAPLUS

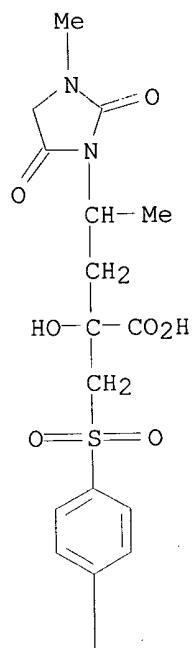
CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[[[(5-methyl-3-isoxazolyl)methyl]thio]methyl]- (9CI) (CA INDEX NAME)



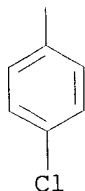
RN 226420-02-6 CAPLUS

CN Pentonic acid, 2-C-[[[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]methyl]-3,4,5-trideoxy-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)- (9CI) (CA INDEX NAME)

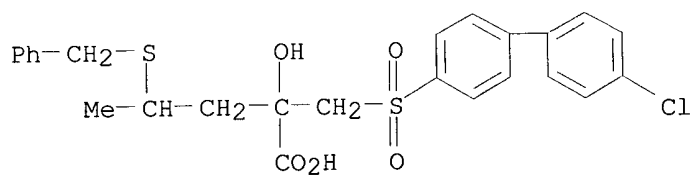
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PAGE 2-A

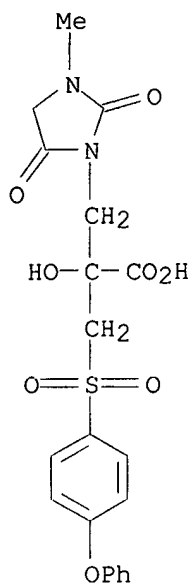


RN 226420-03-7 CAPLUS  
 CN Pentonic acid, 2-C-[[4-(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]methyl]-3,5-dideoxy-4-S-(phenylmethyl)-4-thio- (9CI) (CA INDEX NAME)



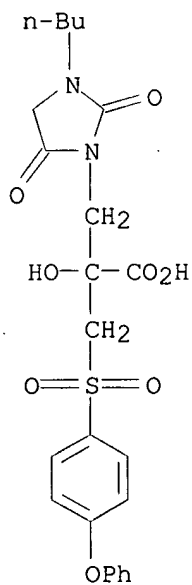
RN 226420-04-8 CAPLUS  
 CN 1-Imidazolidinepropanoic acid, .alpha.-hydroxy-3-methyl-2,5-dioxo-.alpha.-[[4-(4-phenoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)





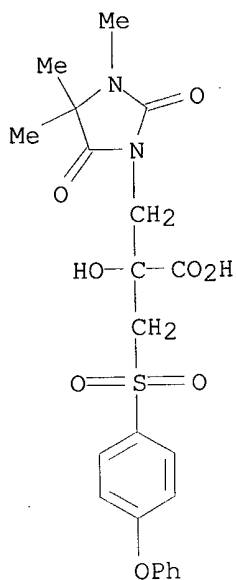
RN 226420-05-9 CAPLUS

CN 1-Imidazolidinepropanoic acid, 3-butyl-.alpha.-hydroxy-2,5-dioxo-.alpha.-  
[[ (4-phenoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)

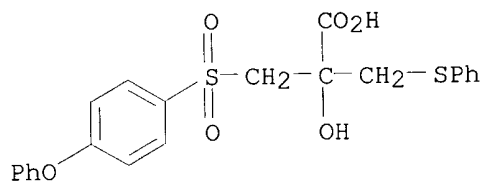


RN 226420-06-0 CAPLUS

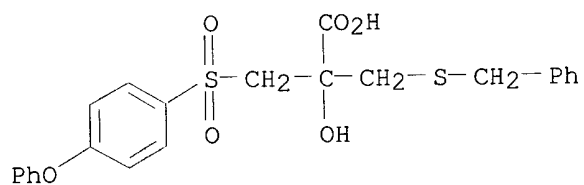
CN 1-Imidazolidinepropanoic acid, .alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-  
.alpha.-[[ (4-phenoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)



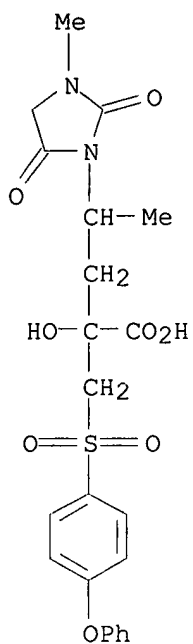
RN 226420-07-1 CAPLUS  
 CN Propanoic acid, 2-hydroxy-2-[[ (4-phenoxyphenyl)sulfonyl]methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



RN 226420-08-2 CAPLUS  
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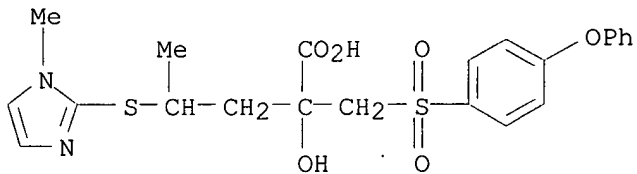


RN 226420-09-3 CAPLUS  
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RN 226420-10-6 CAPLUS

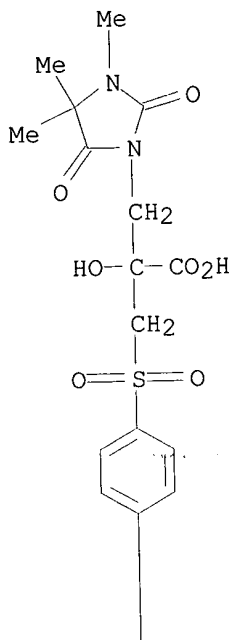
CN Pentonic acid, 3,5-dideoxy-4-S-(1-methyl-1H-imidazol-2-yl)-2-C-[[4-phenoxyphenyl)sulfonyl)methyl]-4-thio- (9CI) (CA INDEX NAME)



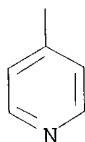
RN 226420-11-7 CAPLUS

CN 1-Imidazolidinepropanoic acid, .alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-.alpha.-[[[4-(4-pyridinyl)phenyl)sulfonyl)methyl]- (9CI) (CA INDEX NAME)

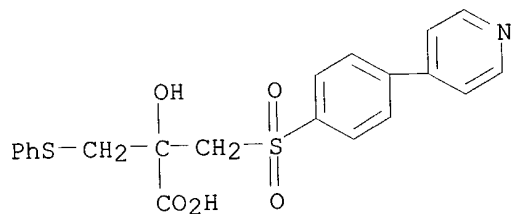
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PAGE 2-A

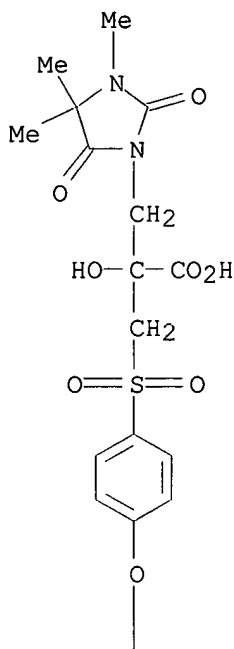


RN 226420-12-8 CAPLUS  
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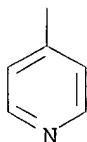


RN 226420-13-9 CAPLUS  
 CN 1-Imidazolidinepropanoic acid, .alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-.alpha.-[[[4-(4-pyridinyloxy)phenyl]sulfonyl]methyl]- (9CI) (CA INDEX NAME)

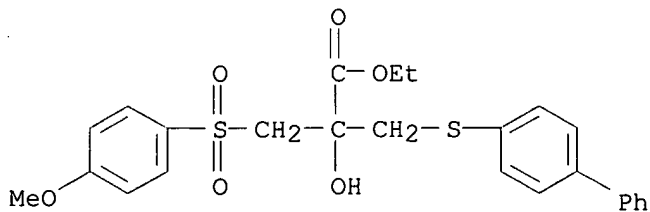
PAGE 1-A



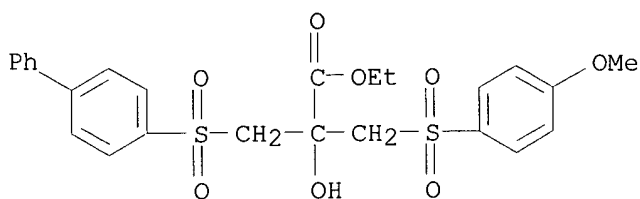
PAGE 2-A



IT 226420-16-2P 226420-17-3P 226420-18-4P  
 226420-20-8P 226420-21-9P 226420-22-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prepn. of .alpha.-hydroxy, -amino, and halo derivs. of .beta.-sulfonyl  
 hydroxamic acids as matrix metalloproteinases inhibitors)  
 RN 226420-16-2 CAPLUS  
 CN Propanoic acid, 3-([1,1'-biphenyl]-4-ylthio)-2-hydroxy-2-[[4-  
 methoxyphenyl)sulfonyl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)

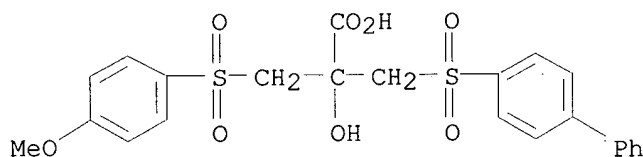


RN 226420-17-3 CAPLUS  
 CN Propanoic acid, 3-([1,1'-biphenyl]-4-ylsulfonyl)-2-hydroxy-2-[[4-  
 methoxyphenyl)sulfonyl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)



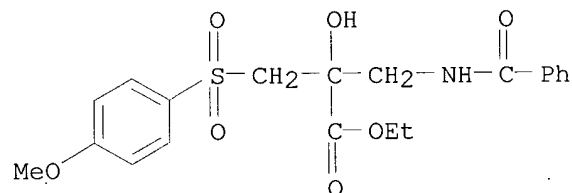
RN 226420-18-4 CAPLUS

CN Propanoic acid, 3-([1,1'-biphenyl]-4-ylsulfonyl)-2-hydroxy-2-[[4-methoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)



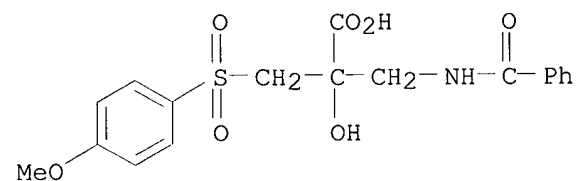
RN 226420-20-8 CAPLUS

CN Propanoic acid, 3-(benzoylamino)-2-hydroxy-2-[[4-methoxyphenyl)sulfonyl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)



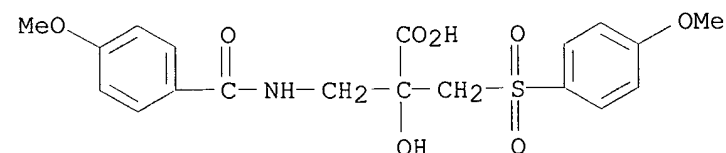
RN 226420-21-9 CAPLUS

CN Propanoic acid, 2-hydroxy-3-[(4-methoxybenzoyl)amino]-2-[[4-methoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)



RN 226420-22-0 CAPLUS

CN Propanoic acid, 2-hydroxy-3-[(4-methoxybenzoyl)amino]-2-[[4-methoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)



L17 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:612095 CAPLUS

DOCUMENT NUMBER: 129:244921

TITLE: Preparation of aromatic sulfonyl alpha-hydroxy hydroxamic acid compounds as matrix metalloprotease inhibitors

INVENTOR(S): Freskos, John N.; Boehm, Terri L.; Mischke, Brent V.; Heintz, Robert M.; McDonald, Joseph J.; Decrescenzo, Gary A.; Howard, Susan C.

PATENT ASSIGNEE(S): Monsanto Company, USA

SOURCE: PCT Int. Appl., 203 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9839326	A1	19980911	WO 1998-US4277	19980304
W:	AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9864478	A1	19980922	AU 1998-64478	19980304
AU 737329	B2	20010816		
EP 984959	A1	20000315	EP 1998-910177	19980304
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
BR 9808150	A	20000328	BR 1998-8150	19980304
JP 2002515900	T2	20020528	JP 1998-537985	19980304
US 6362183	B1	20020326	US 1999-254535	19990604
US 2002173508	A1	20021121	US 2001-5437	20011203
PRIORITY APPLN. INFO.:			US 1997-35182P	P 19970304
			WO 1998-US4277	W 19980304
			US 1999-254535	A1 19990604

OTHER SOURCE(S): MARPAT 129:244921

AB The title compds. HONHC(O)C(OH)(R2)CH2SO2R1 [I; R2 = H, C1-4 alkyl, C1-4 haloalkyl, etc.; R1 = 5-6 membered cycloalkyl, heterocyclyl, aryl, etc.] which inter alia inhibit matrix metalloprotease activity, were prepd. Thus, multi-step synthesis of I [R1 = 4-PhOC6H4; R2 = Me] which showed 51.9% inhibition of angiogenesis in the cornea of a mouse, was described.

IT 213184-22-6P 213184-23-7P 213184-27-1P

213184-30-6P 213184-31-7P 213184-32-8P

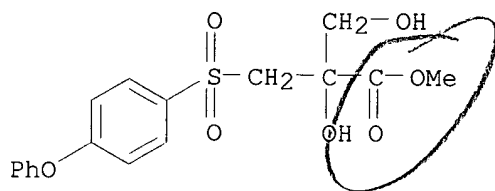
213184-47-5P 213184-48-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

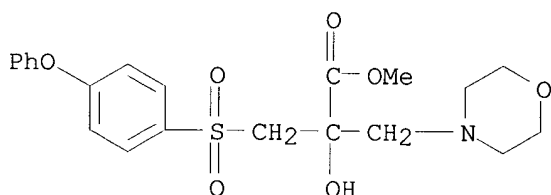
(prepn. of arom. sulfonyl alpha-hydroxy hydroxamic acid compds. as matrix metalloprotease inhibitors)

RN 213184-22-6 CAPLUS

CN Propanoic acid, 2,3-dihydroxy-2-[[[4-phenoxyphenyl)sulfonyl)methyl]-, methyl ester (9CI) (CA INDEX NAME)

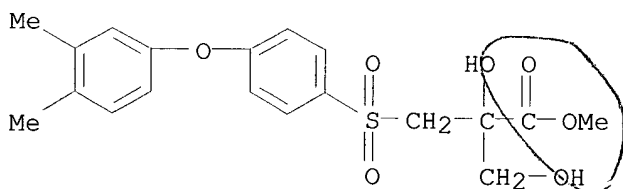


RN 213184-23-7 CAPLUS  
 CN 4-Morpholinepropanoic acid, .alpha.-hydroxy-.alpha.-[[4-phenoxyphenyl)sulfonyl]methyl]-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)

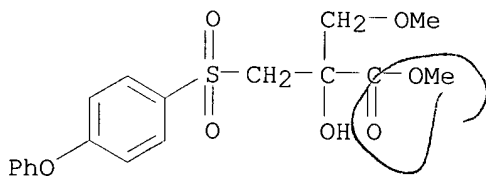


● HCl

RN 213184-27-1 CAPLUS  
 CN Propanoic acid, 3-[[4-(3,4-dimethylphenoxy)phenyl)sulfonyl]-2-hydroxy-2-(hydroxymethyl)-, methyl ester (9CI) (CA INDEX NAME)

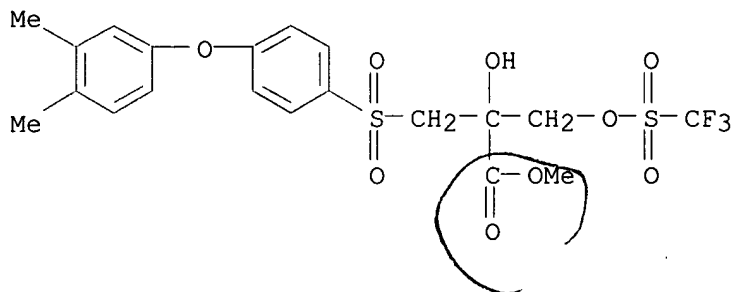


RN 213184-30-6 CAPLUS  
 CN Propanoic acid, 2-hydroxy-2-(methoxymethyl)-3-[[4-(3,4-dimethylphenoxy)phenyl)sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

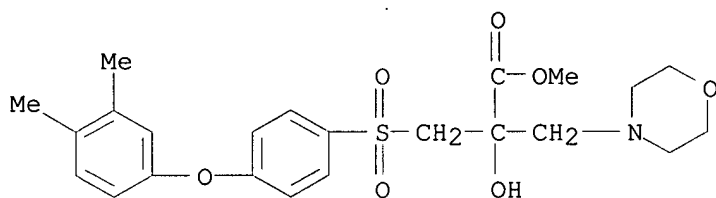


RN 213184-31-7 CAPLUS  
 CN Propanoic acid, 3-[[4-(3,4-dimethylphenoxy)phenyl)sulfonyl]-2-hydroxy-2-[[[(trifluoromethyl)sulfonyl]oxy]methyl]-, methyl ester (9CI) (CA INDEX NAME)



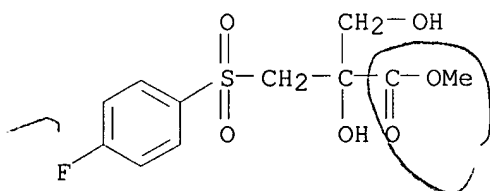


RN 213184-32-8 CAPLUS  
CN 4-Morpholinepropanoic acid, .alpha.-[[[4-(3,4-dimethylphenoxy)phenyl]sulfonyl]methyl]-.alpha.-hydroxy-, methyl ester, hydrochloride (9CI) (CA INDEX NAME)

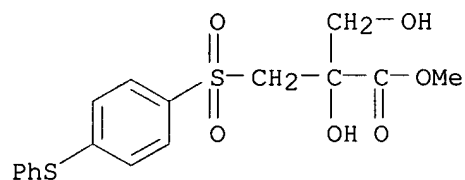


● HCl

RN 213184-47-5 CAPLUS  
CN Propanoic acid, 3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-(hydroxymethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 213184-48-6 CAPLUS  
CN Propanoic acid, 2,3-dihydroxy-2-[[[4-(phenylthio)phenyl]sulfonyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1968:418764 CAPLUS  
DOCUMENT NUMBER: 69:18764

Searched by Barb O'Bryen, STIC 308-4291

TITLE: Some reactions of ethyl .beta.-(p-aminophenylsulfonyl)-  
.alpha.-nitropropionate  
AUTHOR(S): Mikheeva, L. F.; Lisova, V. S.; Dmitrenko, V. N.  
CORPORATE SOURCE: Leningrad. Khim.-Farm. Inst., Leningrad, USSR  
SOURCE: Zhurnal Organicheskoi Khimii (1968), 4(5), 834-6  
CODEN: ZORKAE; ISSN: 0514-7492

DOCUMENT TYPE: Journal  
LANGUAGE: Russian

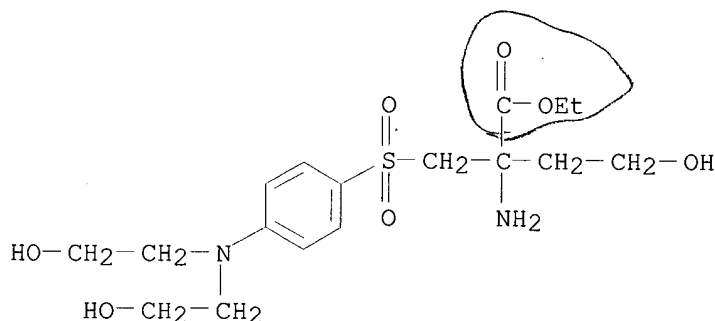
AB The structure of p-H<sub>2</sub>N-C<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>CH(NO<sub>2</sub>)CO<sub>2</sub>Et (I), which was prepd. by L. F. Mikheeva in 1963, is further corroborated by its chem. reactions. Redn. and simultaneous hydrolysis of I gave p-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H. Action of ethylene oxide in aq. soln. on I gave p-(HCOCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>CH(NO<sub>2</sub>)CO<sub>2</sub>Et (II) and a small amt. of p-(HOCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>CH(NO<sub>2</sub>)(CH<sub>2</sub>CH<sub>2</sub>OH)CO<sub>2</sub>Et which was reduced to p-(HOCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>CH(NH<sub>2</sub>)(CH<sub>2</sub>CH<sub>2</sub>OH)CO<sub>2</sub>Et. Redn. of II also proceeded with simultaneous hydrolysis; p-(HOCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H (IV) was obtained. The reaction of IV.2HCl with SOCl<sub>2</sub> gave p-(ClCH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>CH(NH<sub>2</sub>.HCl)CO<sub>2</sub>H.

IT 18739-89-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 18739-89-4 CAPLUS

CN Butyric acid, 2-amino-2-[[N,N-bis(2-hydroxyethyl)sulfanilyl]methyl]-4-hydroxy-, ethyl ester (8CI) (CA INDEX NAME)



L17 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1961:13184 CAPLUS

DOCUMENT NUMBER: 55:13184

ORIGINAL REFERENCE NO.: 55:2545c-i,2546a

TITLE: The oxidative addition of mercaptans to olefins in the presence of halide

AUTHOR(S): Bredereck, Hellmut; Wagner, Adolf; Kottenhahn, Alfred

CORPORATE SOURCE: Tech. Hochschule, Stuttgart, Germany

SOURCE: Chem. Ber. (1960), 93, 2415-23

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB The prepn. of a series of .beta.-hydroxysulfoxides by oxidative addn. of mercaptans to olefins was described; the reaction was strongly catalyzed by chloride or bromide. The prepn. were performed by the method described previously (CA 54, 3290a). PhSH (1.17 g.) and 1.25 cc. styrene (I) in 10 cc. heptane at 30.degree. yielded 0.6 g. PhSOCH<sub>2</sub>CHPhOH (II), m. 131.5.degree. (C<sub>6</sub>H<sub>6</sub>). II treated with shaking with excess aq. KMnO<sub>4</sub>, treated with a few drops H<sub>2</sub>O<sub>2</sub>, dild. with H<sub>2</sub>O, and the product isolated with CHCl<sub>3</sub> yielded 50% PhSO<sub>2</sub>CH<sub>2</sub>CHPhOH, m. 94-5.degree.. p-MeC<sub>6</sub>H<sub>4</sub>SH (223 mg.) and 0.22 cc. I in 10 cc. heptane at 30.degree. gave 342 mg. p-MeC<sub>6</sub>H<sub>4</sub>SOCH<sub>2</sub>CHPhOH, m. 110-11.degree. (C<sub>6</sub>H<sub>6</sub>-petr. ether). PhCH<sub>2</sub>SH (1.02 g.) and 4 cc. I in 10 cc. heptane at 30.degree. yielded 450 mg. PhCH<sub>2</sub>SOCH<sub>2</sub>CHPhOH, m. 168-9.degree. (C<sub>6</sub>H<sub>6</sub>). I (2.6 g.) and 2.27 g. Me<sub>3</sub>CSH

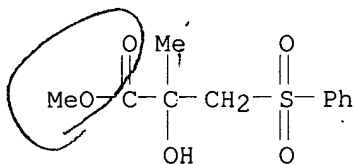
at 25.degree. gave similarly 2.03 g. crude product, which, fractionally crystd. from C6H6, gave 650 mg. Me3CSOCH2CHPhOH, needles, m. 137-8.degree., and 415 mg. low-melting modification, cubes, m. 112-12.5.degree.; both modifications oxidized with aq. KMnO4 gave Me3CSO2CH2CHPhOH, needles, m. 112.5-13.degree. (C6H6petr. ether). PhSH (11 g.) and 10 g. CH2:CMcCO2Me in 50 cc. heptane yielded PhSOCH2CMe(OH)CO2Me, m. 90-1.degree. (C6H6); sulfone analog (II) m. 68-9.5.degree. (C6H6-petr. ether). PhSCH2CMe(OH)CO2H (2.5 g.) with CH2N2-Et2O yielded the Me ester, b0.03 102-3.degree., which, oxidized with aq. KMnO4, yielded II, m. 68-9.5.degree.. p-MeC6H4SH (12.4 g.) and 10 g. CH2:CMcCO2Me in 50 cc. heptane gave 24.3 g. p-MeC6H4SOCH2CMe(OH)CO2Me (III), m. 58-60.degree. (Et2O-petr. ether). III (5.4 g.) oxidized with KMnO4 yielded 4.7 g. sulfone analog, m. 80-1.degree. (abs. EtOH). p-MeC6H6SH (1.06 g.) in 30 cc. MeCH:CHCO2Me at 35.degree. gave 0.5 g. crude material; 3.3 g. crude product fractionally recrystd. from C6H6 yielded 1.4 g. p-MeC6H4SOCHMeCH(OH)CO2Me (IV), m. 134-5.degree., and 0.8 g. low-melting modification, needles, m. 123-4.degree. (C6H6petr. ether). IV, m. 124.degree., (256 mg.) in 3 cc. glacial AcOH oxidized with 108 mg. KMnO4 yielded 210 mg. sulfonyl analog of IV, needles, m. 79.5-80.5.degree. (EtOH), which was also obtained from IV, m. 135.degree.. p-MeC6H4SH (228 mg.) and 0.4 cc. CH2:CMcCN in 10 cc. heptane at 35.degree. yielded 325 mg. p-MeC6H4SOCH2C(OH)(CN)Me (V), m. 119-21.degree. (pptd. from C6H6 with petr. ether). V (1.22 g.), 1.3 cc. 30% H2O2, and 10 cc. glacial AcOH kept 4 days at room temp. gave 1.2 g. sulfonyl analog of V, m. 109-12.degree. (C6H6-AcOH). V (1.42 g.), 1.5 cc. 30% H2O2, and 10 cc. glacial AcOH heated 3 hrs. at 100.degree. gave 370 mg. p-MeC6H4SO2CH2Ac (VI), m. 50-1.degree. (Et2O-petr. ether); the Et2O-insol. residue recrystd. from EtOH gave 270 mg. p-MeC6H4SO2CH2C(OH)(CONH2)Me, m. 175-5.5.degree., and about 0.3 g. p-MeC6H4SO3NH4, m. 330.degree. (decompn.). V (2.9 g.) oxidized with 1.4 g. KMnO4 in glacial AcOH yielded 1.55 g. VI, m. 51-2.degree. (Et2O-petr. ether). p-MeC6H4SH (1.53 g.) and 3 cc. CH2:CHCO2Me in 30 cc. heptane at 35.degree. yielded 1.03 g. (crude) p-MeC6H4SOCH2CH(OH)CO2Me, m. 106-7.degree. (C6H6), and a 2nd modification, needles, m. 80-1.degree. (C6H6-petr. ether); both modifications oxidized with 30% H2O2 gave 95% of the same sulfone analog, needles, m. 88-8.5.degree. (EtOH). PhSH (537 mg.) in 100 cc. cyclohexene at 25.degree. gave 100 mg. 2-phenylsulfinylcyclohexanol, m. 156-6.5.degree. (C6H6); sulfone analog m. 110-10.5.degree. (C6H6-petr. ether). PhSH (284 mg.) in 5 cc. CH2:CHCN at 30.degree. gave 253 mg. PhSOCH2CH(OH)CN, m. 108-10.degree.; sulfone analog, 85%, m. 107-8.degree. (C6H6).

IT 100059-74-3, Lactic acid, 2-methyl-3-(phenylsulfonyl)-, methyl ester

(prepn. of)

RN 100059-74-3 CAPLUS

CN Lactic acid, 2-methyl-3-(phenylsulfonyl)-, methyl ester (6CI) (CA INDEX NAME)



L17 ANSWER 7 OF 7 USPATFULL

ACCESSION NUMBER: 2002:209710 USPATFULL

TITLE: .alpha.-hydroxy, -amino, and halo derivatives of  
.beta.-sulfonyl hydroxamic acids as matrix  
metalloproteinases inhibitors

INVENTOR(S): Warpehoski, Martha A., 7600 Curry La., Portage, MI,  
United States 49024

Mitchell, Mark Allen, 1628 Dover Rd., Kalamazoo, MI,  
United States 49008  
Harper, Donald E., 11520 Channel Dr., Plainwell, MI,  
United States 49080  
Maggiora, Linda Louise, 4400 Glenrose Ter., Kalamazoo,  
MI, United States 49008

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6437177	B1	20020820
APPLICATION INFO.:	US 1998-196190		<u>19981120</u> (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-72655P	19971121 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Shah, Mukund J.	
ASSISTANT EXAMINER:	McKenzie, Thomas	
LEGAL REPRESENTATIVE:	Oblon, Spivak, McClelland, Maier & Neustadt, P.C.	
NUMBER OF CLAIMS:	13	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)	
LINE COUNT:	1254	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a compound of formula I ##STR1##

or pharmaceutical acceptable salts thereof wherein R.sub.1 is C.sub.4-12 alkyl, C.sub.4-12 alkenyl, C.sub.4-12 alkynyl, --(CH.sub.2).sub.h-- C.sub.3-8 cycloalkyl, substituted and unsubstituted --(CH.sub.2).sub.h-aryl, substituted and unsubstituted --(CH.sub.2).sub.h-het, R.sub.2 is substituted and unsubstituted C.sub.1-12 alkyl, substituted and unsubstituted C.sub.2-12 alkenyl, substituted and unsubstituted C.sub.2-12 alkynyl, substituted and unsubstituted --(CH.sub.2).sub.h-- C.sub.3-8 cycloalkyl, substituted and unsubstituted --(CH.sub.2).sub.h-- C.sub.3-8 cycloalkenyl, substituted and unsubstituted --(CH.sub.2).sub.h-aryl, substituted and unsubstituted --(CH.sub.2).sub.h-heterocyclic ring, substituted and unsubstituted --(CH.sub.2).sub.i--X--R.sub.4 (X is --O--, --S(.dbd.O).sub.j--, --NR.sub.7--, --S(.dbd.O).sub.2NR.sub.8--, or --C(.dbd.O)--), and --(CH.sub.2).sub.iCHR.sub.5R.sub.6.

The compounds are inhibitors of matrix metalloproteinases involved in tissue degradation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 226419-90-5P 226419-91-6P 226419-92-7P

226419-93-8P 226419-94-9P 226419-95-0P

226419-96-1P 226419-97-2P 226419-98-3P

226419-99-4P 226420-00-4P 226420-01-5P

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226420-05-9P 226420-06-0P 226420-07-1P

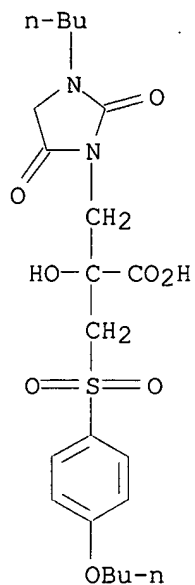
226420-08-2P 226420-09-3P 226420-10-6P

226420-11-7P 226420-12-8P 226420-13-9P

(prepn. of .alpha.-hydroxy, -amino, and halo derivs. of .beta.-sulfonyl hydroxamic acids as matrix metalloproteinases inhibitors)

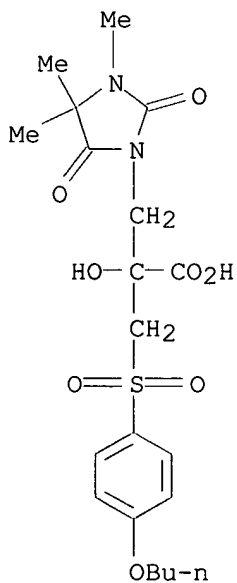
RN 226419-90-5 USPTFULL

CN 1-Imidazolidinepropanoic acid, .alpha.-[[ (4-butoxyphenyl)sulfonyl]methyl]-3-butyl-.alpha.-hydroxy-2,5-dioxo- (9CI) (CA INDEX NAME)



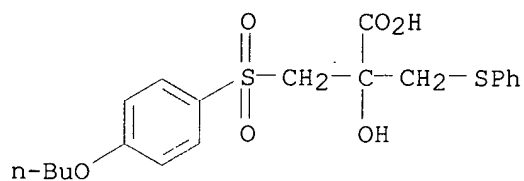
RN 226419-91-6 USPATFULL

CN 1-Imidazolidinepropanoic acid, .alpha.-[[ (4-butoxyphenyl)sulfonyl]methyl]-  
.alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo- (9CI) (CA INDEX NAME)



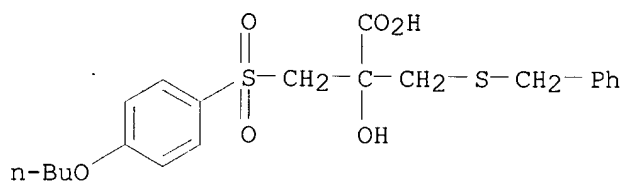
RN 226419-92-7 USPATFULL

CN Propanoic acid, 3-[[ (4-butoxyphenyl)sulfonyl]-2-hydroxy-2-  
[(phenylthio)methyl]- (9CI) (CA INDEX NAME)



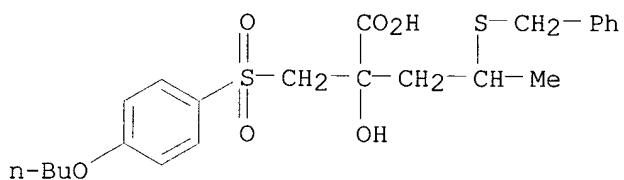
RN 226419-93-8 USPATFULL

CN Propanoic acid, 3-[(4-butoxyphenyl)sulfonyl]-2-hydroxy-2-  
[[ (phenylmethyl)thio]methyl]- (9CI) (CA INDEX NAME)



RN 226419-94-9 USPATFULL

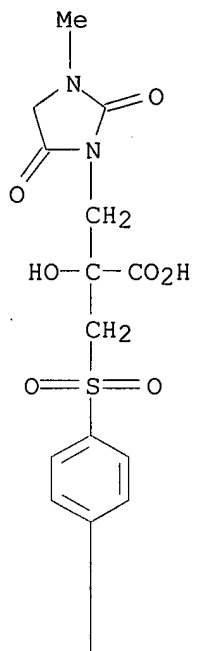
CN Pentonic acid, 2-C-[[ (4-butoxyphenyl)sulfonyl]methyl]-3,5-dideoxy-4-S-  
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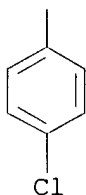
RN 226419-95-0 USPATFULL

CN 1-Imidazolidinepropanoic acid, .alpha.-[[ (4'-chloro[1,1'-biphenyl]-4-  
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NAME)

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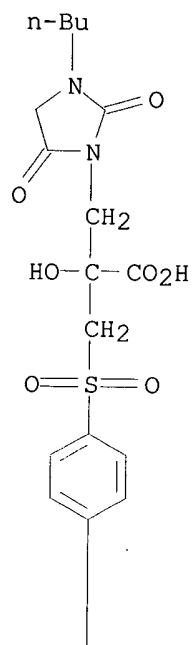


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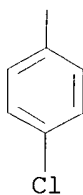


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CN 1-Imidazolidinepropanoic acid, 3-butyl-.alpha.-[[[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]methyl]-.alpha.-hydroxy-2,5-dioxo- (9CI) (CA INDEX NAME)

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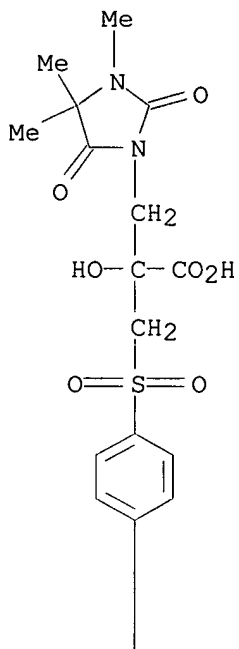
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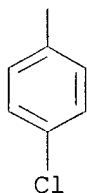
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CN 1-Imidazolidinepropanoic acid, .alpha.-[[[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]methyl]-.alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo- (9CI)  
(CA INDEX NAME)



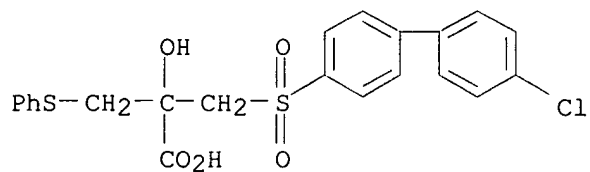
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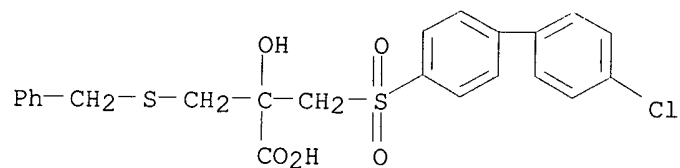


RN 226419-98-3 USPATFULL

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[(phenylthio)methyl]- (9CI) (CA INDEX NAME)

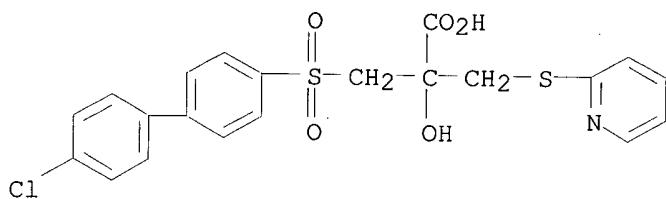
RN 226419-99-4 USPATFULL

CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-  
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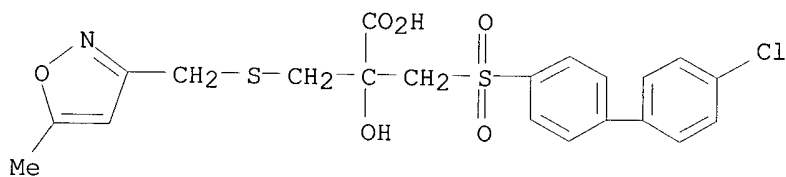
RN 226420-00-4 USPATFULL

CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[(2-pyridinylthio)methyl]- (9CI) (CA INDEX NAME)



RN 226420-01-5 USPATFULL

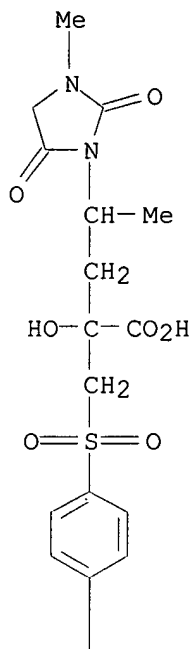
CN Propanoic acid, 3-[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]-2-hydroxy-2-[[[(5-methyl-3-isoxazolyl)methyl]thio]methyl]- (9CI) (CA INDEX NAME)



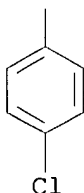
RN 226420-02-6 USPATFULL

CN Pentonic acid, 2-C-[[[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]methyl]-3,4,5-trideoxy-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)- (9CI) (CA INDEX NAME)

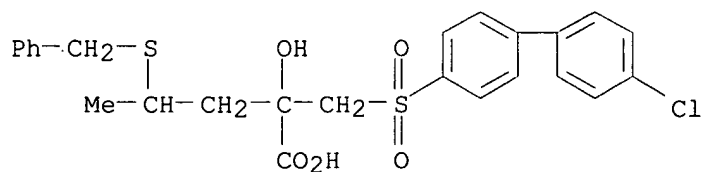
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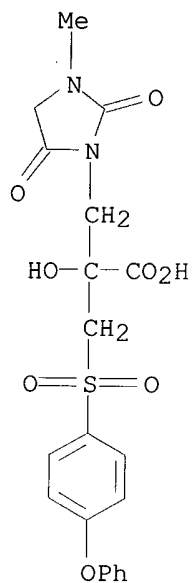
PAGE 2-A



RN 226420-03-7 USPATFULL  
 CN Pentonic acid, 2-C-[[ (4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]methyl]-3,5-dideoxy-4-S-(phenylmethyl)-4-thio- (9CI) (CA INDEX NAME)

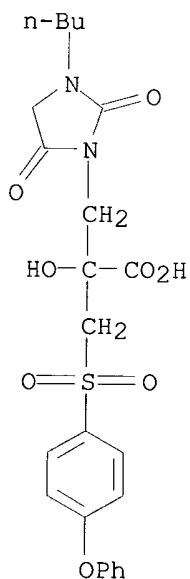


RN 226420-04-8 USPATFULL  
 CN 1-Imidazolidinepropanoic acid, .alpha.-hydroxy-3-methyl-2,5-dioxo-.alpha.-[[ (4-phenoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)



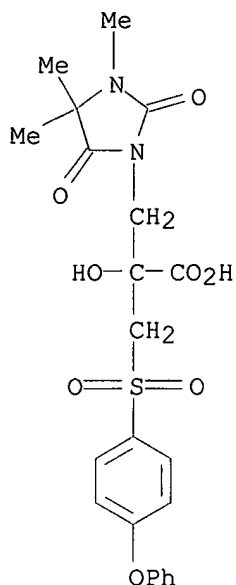
RN 226420-05-9 USPATFULL

CN 1-Imidazolidinepropanoic acid, 3-butyl-.alpha.-hydroxy-2,5-dioxo-.alpha.-  
[[ (4-phenoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)



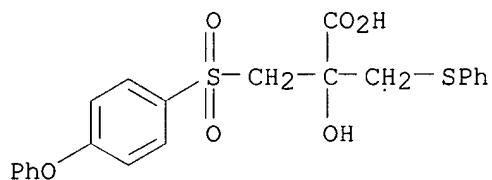
RN 226420-06-0 USPATFULL

CN 1-Imidazolidinepropanoic acid, .alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-.  
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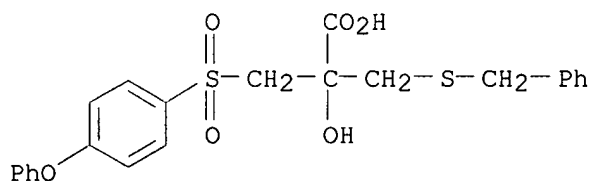
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CN Propanoic acid, 2-hydroxy-2-[[[4-phenoxyphenyl)sulfonyl)methyl]-3-(phenylthio)- (9CI) (CA INDEX NAME)



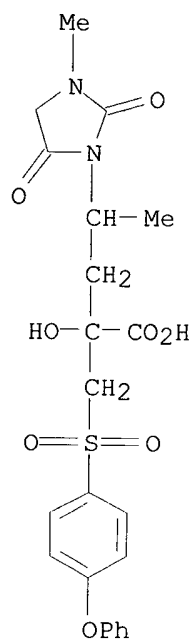
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CN Propanoic acid, 2-hydroxy-2-[[[4-phenoxyphenyl)sulfonyl)methyl]-3-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)



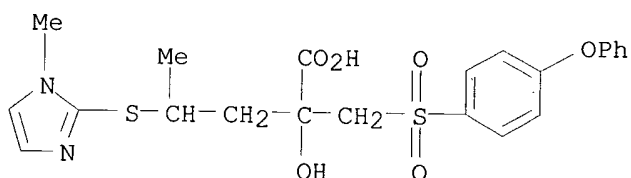
RN 226420-09-3 USPATFULL

CN Pentonic acid, 3,4,5-trideoxy-4-(3-methyl-2,5-dioxo-1-imidazolidinyl)-2-C-[[[4-phenoxyphenyl)sulfonyl)methyl]- (9CI) (CA INDEX NAME)



RN 226420-10-6 USPATFULL

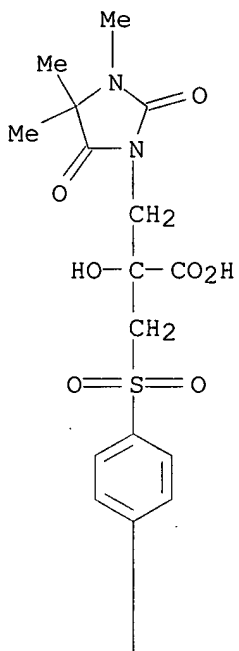
CN Pentonic acid, 3,5-dideoxy-4-S-(1-methyl-1H-imidazol-2-yl)-2-C-[[4-phenoxyphenyl)sulfonyl]methyl]-4-thio- (9CI) (CA INDEX NAME)



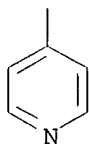
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CN 1-Imidazolidinepropanoic acid, .alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-.alpha.-[[[4-(4-pyridinyl)phenyl]sulfonyl]methyl]- (9CI) (CA INDEX NAME)

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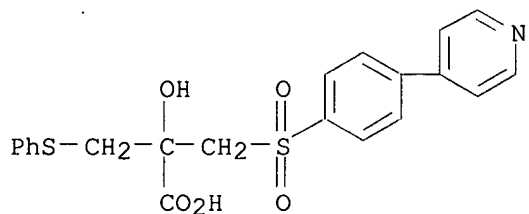


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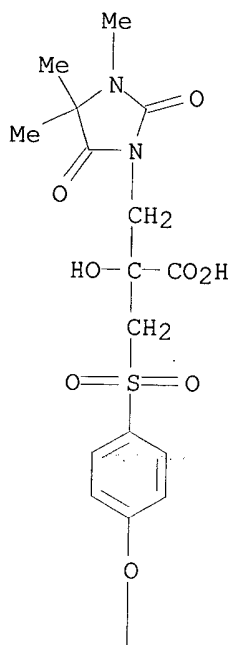
CN Propanoic acid, 2-hydroxy-2-[(phenylthio)methyl]-3-[[4-(4-pyridinyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



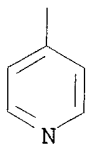
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CN 1-Imidazolidinepropanoic acid, .alpha.-hydroxy-3,4,4-trimethyl-2,5-dioxo-.alpha.-[[[4-(4-pyridinyloxy)phenyl]sulfonyl]methyl]- (9CI) (CA INDEX NAME)

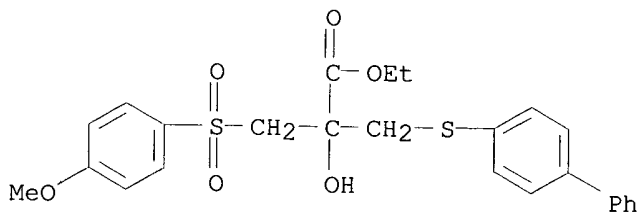
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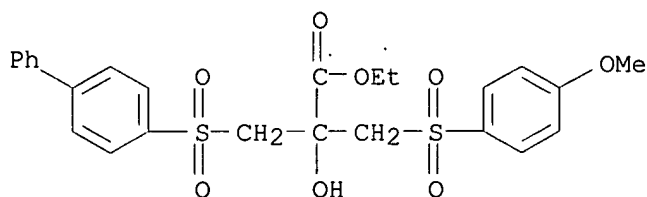


IT 226420-16-2P 226420-17-3P 226420-18-4P  
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 hydroxamic acids as matrix metalloproteinases inhibitors)  
 RN 226420-16-2 USPATFULL  
 CN Propanoic acid, 3-([1,1'-biphenyl]-4-ylthio)-2-hydroxy-2-[[4-  
 methoxyphenyl)sulfonyl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)



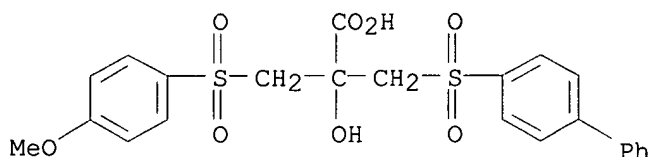
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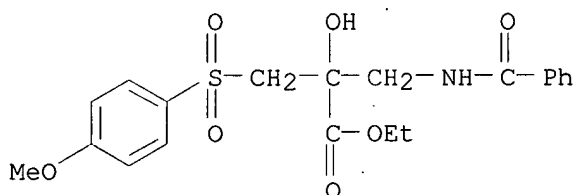
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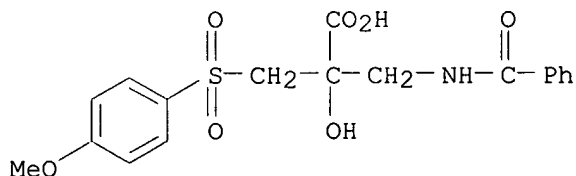
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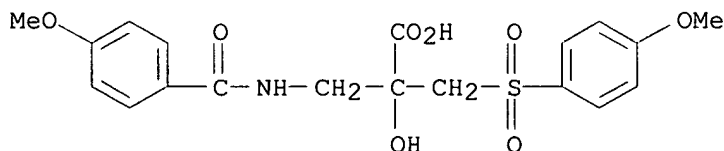
RN 226420-21-9 USPATFULL

CN Propanoic acid, 2-hydroxy-3-[(4-methoxybenzoyl)amino]-2-[[4-methoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)



RN 226420-22-0 USPATFULL

CN Propanoic acid, 2-hydroxy-3-[(4-methoxybenzoyl)amino]-2-[[4-methoxyphenyl)sulfonyl]methyl]- (9CI) (CA INDEX NAME)



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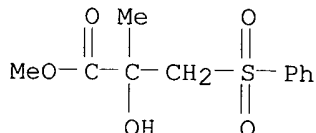
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TITLE: oxidative addn. of mercaptans to olefins in the presence of  
          halide  
AUTHOR NAME: Brederick, Hellmut; Wagner, A.; Kottenhahn, A.  
INDEX TERM: 5366-49-4 41103-87-1 41851-76-7 49639-26-1 51755-92-1  
          56706-30-0 59871-21-5 59871-23-7 64454-43-9 99855-90-0  
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IT **100059-74-3**  
RN 100059-74-3 CAOLD  
CN Lactic acid, 2-methyl-3-(phenylsulfonyl)-, methyl ester (6CI) (CA INDEX  
NAME)



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study of the rates of isotope exchange of S in *m*-(I) and *p*-chlorobenzenesulfonic acid (II) with radioactive 79.5%  $\text{H}_2\text{SO}_4$ , the monomol. const. of the rates of reactions of hydrolysis of both isomers were found for various temps. [the temp., strength of  $\text{H}_2\text{SO}_4$  in the mixt. (%), no. of moles of  $\text{H}_2\text{SO}_4$ /mole of sulfonic acid, and  $k$  (in  $\text{hr}^{-1}$ ) given]. For I: 185.5, 78.9, 3.55,  $0.0042 \pm 0.0001$ ; 201.0, 79.4, 3.64,  $0.0186 \pm 0.0002$ ; 220.0, 79.4, 3.64,  $0.81 \pm 0.003$ . For II: 160.5, 78.3, 3.63,  $0.044 \pm 0.004$ ; 170.0, 79.6, 3.50,  $0.099 \pm 0.002$ ; 185.5, 79.0, 3.75,  $0.324 \pm 0.001$ ; 185.5, 78.3, 3.63,  $0.300 \pm 0.005$ . The log of the mean values of the rate const. depended linearly on the reciprocal of the temp. The mean values of the activation energy after the hydrolysis reactions of both isomers and the preexponential members of the Arrhenius equation were given for I and II, resp.:  $E = 28 \pm 2$  and  $31 \pm 2$  kcal./mole,  $\log N$  ( $N$  in  $\text{hr}^{-1}$ ) =  $16 \pm 1$  and  $14 \pm 1$ . A comparison of the results of the kinetic study of the hydrolysis and isomerization reactions of I and II proved the intermol. nature of the isomerization reaction. The rel. rates of sulfonation of PhCl at the *m*- and *p*-position were estd. quant. It was possible to calc. the rates of the isomerization reactions from the equil. const. between the isomers and from the rate const. of the hydrolysis reactions. Jean Plamondon

The oxidative addition of mercaptans to olefins in the presence of halide. Hellmut Bredereck, Adolf Wagner, and Alfred Kottenhahn (Tech. Hochschule, Stuttgart, Ger.). *Chem. Ber.* 93, 2415–23 (1960).—The prepn. of a series of  $\beta$ -hydroxysulfoxides by oxidative addn. of mercaptans to olefins was described; the reaction was strongly catalyzed by chloride or bromide. The preps. were performed by the method described previously (CA 54, 3290a). PhSH (1.17 g.) and 1.25 cc. styrene (I) in 10 cc. heptane at  $30^\circ$  yielded 0.6 g. PhSOCH<sub>2</sub>CHPhOH (II), m.  $131.5^\circ$  ( $\text{C}_6\text{H}_5$ ). II treated with shaking with excess aq.  $\text{KMnO}_4$ , treated with a few drops  $\text{H}_2\text{O}_2$ , dild. with  $\text{H}_2\text{O}$ , and the product isolated with  $\text{CHCl}_3$  yielded 50% PhSO<sub>2</sub>CH<sub>2</sub>CHPhOH, m.  $94-5^\circ$ . *p*-MeC<sub>6</sub>H<sub>4</sub>SH (223 mg.) and 0.22 cc. I in 10 cc. heptane at  $30^\circ$  gave 342 mg. *p*-MeC<sub>6</sub>H<sub>4</sub>SOCH<sub>2</sub>CHPhOH, m.  $110-11^\circ$  ( $\text{C}_6\text{H}_5$ -petr. ether). PhCH<sub>2</sub>SH (1.02 g.) and 4 cc. I in 10 cc. heptane at  $30^\circ$  yielded 450 mg. PhCH<sub>2</sub>SOCH<sub>2</sub>CHPhOH, m.  $168-9^\circ$  ( $\text{C}_6\text{H}_5$ ). I (2.6 g.) and 2.27 g. Me<sub>2</sub>CSH at  $25^\circ$  gave similarly 2.03 g. crude product, which, fractionally crystd. from  $\text{C}_6\text{H}_6$ , gave 650 mg. Me<sub>2</sub>CSOCH<sub>2</sub>CHPhOH, needles, m.  $137-8^\circ$ , and 415 mg. low-melting modification, cubes, m.  $112-12.5^\circ$ ; both modifications oxidized with aq.  $\text{KMnO}_4$  gave Me<sub>2</sub>CSO<sub>2</sub>CH<sub>2</sub>CHPhOH, needles, m.  $112.5-13^\circ$  ( $\text{C}_6\text{H}_5$ -petr. ether). PhSH (11 g.) and 10 g. CH<sub>2</sub>:CMeCO<sub>2</sub>Me in 50 cc. heptane yielded PhSOCH<sub>2</sub>CMe(OH)CO<sub>2</sub>Me, m.  $90-1^\circ$  ( $\text{C}_6\text{H}_5$ ); sulfone analog (II) m.  $68-9.5^\circ$  ( $\text{C}_6\text{H}_5$ -petr. ether). PhSH<sub>2</sub>CMe(OH)CO<sub>2</sub>H (2.5 g.) with CH<sub>2</sub>N<sub>2</sub>-Et<sub>2</sub>O yielded the Me ester, b.p.  $102-3^\circ$ , which, oxidized with aq.  $\text{KMnO}_4$ , yielded II, m.  $68-9.5^\circ$ . *p*-MeC<sub>6</sub>H<sub>4</sub>SH (12.4 g.) and 10 g. CH<sub>2</sub>:CMeCO<sub>2</sub>Me in 50 cc. heptane gave 24.3 g. *p*-MeC<sub>6</sub>H<sub>4</sub>SOCH<sub>2</sub>CMe(OH)CO<sub>2</sub>Me (III), m.  $58-60^\circ$  (Et<sub>2</sub>O-petr. ether). III (5.4 g.) oxidized with  $\text{KMnO}_4$  yielded 4.7 g. sulfone analog, m.  $80-1^\circ$  (abs. EtOH). *p*-MeC<sub>6</sub>H<sub>4</sub>SH (1.06 g.) in 30 cc. MeCH:CHCO<sub>2</sub>Me at  $35^\circ$  gave 0.5 g. crude material; 3.3 g. crude product fractionally recrystd. from  $\text{C}_6\text{H}_6$  yielded 1.4 g. *p*-MeC<sub>6</sub>H<sub>4</sub>SOCH<sub>2</sub>MeCH(OH)CO<sub>2</sub>Me (IV), m.  $134-5^\circ$ , and 0.8 g. low-melting modification, needles, m.  $123-4^\circ$  ( $\text{C}_6\text{H}_5$ -petr. ether). IV, m.  $124^\circ$ , (256 mg.) in 3 cc. glacial AcOH oxidized with 108 mg.  $\text{KMnO}_4$  yielded 210 mg. sulfonyl analog of IV, needles, m.  $79.5-80.5^\circ$  (EtOH), which was also obtained from IV, m.  $135^\circ$ . *p*-MeC<sub>6</sub>H<sub>4</sub>SH (228 mg.) and 0.4 cc. CH<sub>2</sub>:CMeCN in 10 cc. heptane at  $35^\circ$  yielded 325 mg. *p*-MeC<sub>6</sub>H<sub>4</sub>SOCH<sub>2</sub>C(OH)(CN)Me (V), m.  $119-21^\circ$  (pptd. from  $\text{C}_6\text{H}_6$  with petr. ether). V (1.22 g.), 1.3 cc. 30%  $\text{H}_2\text{O}_2$ , and 10 cc. glacial AcOH kept 4 days at room temp. gave 1.2 g. sulfonyl analog of V, m.  $109-12^\circ$  ( $\text{C}_6\text{H}_5$ -AcOH). V (1.42 g.), 1.5 cc. 30%  $\text{H}_2\text{O}_2$ , and 10 cc. glacial AcOH heated 3 hrs. at  $100^\circ$  gave 370 mg. *p*-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>Ac (VI), m.  $50-1^\circ$  (Et<sub>2</sub>O-petr. ether); the Et<sub>2</sub>O-insol. residue recrystd. from EtOH gave 270 mg. *p*-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>C(OH)(CONH<sub>2</sub>)Me, m.  $175-5.5^\circ$ , and about 0.3 g. *p*-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>NH<sub>2</sub>, m.  $330^\circ$  (decompn.). V (2.9 g.) oxidized with 1.4 g.  $\text{KMnO}_4$  in glacial AcOH yielded 1.55 g. VI, m.  $51-2^\circ$  (Et<sub>2</sub>O-petr. ether). *p*-MeC<sub>6</sub>H<sub>4</sub>SH (1.53 g.) and 3 cc. CH<sub>2</sub>:CHCO<sub>2</sub>Me in 30 cc. heptane at  $35^\circ$  yielded 1.03 g. (crude) *p*-MeC<sub>6</sub>H<sub>4</sub>SOCH<sub>2</sub>CH(OH)CO<sub>2</sub>Me, m.  $106-7^\circ$  ( $\text{C}_6\text{H}_5$ ), and a 2nd modification, needles, m.  $80-1^\circ$  ( $\text{C}_6\text{H}_5$ -petr. ether); both modifications oxidized with 30%  $\text{H}_2\text{O}_2$  gave 95% of the same sulfone analog, needles, m.  $88-8.5^\circ$  (EtOH). PhSH (537

mg.) in 100 cc. cyclohexene at  $25^\circ$  gave 100 mg. 2-phenylsulfinylcyclohexanol, m.  $156-6.5^\circ$  ( $\text{C}_6\text{H}_5$ ); sulfone analog m.  $110-10.5^\circ$  ( $\text{C}_6\text{H}_5$ -petr. ether). PhSH (284 mg.) in 5 cc. CH<sub>2</sub>:CHCN at  $30^\circ$  gave 253 mg. PhSOCH<sub>2</sub>CH(OH)CN, m.  $108-10^\circ$ ; sulfone analog, 85%, m.  $107-8^\circ$  ( $\text{C}_6\text{H}_5$ ).

F. W. Hoffmann

Synthetic antitubercular agents. I. Thiosemicarbazones of  $\alpha$ -(*p*-formylphenylthio) acids and esters. R. Trave (Univ. Milan). *Farmco* (Pavia) Ed. sci. 15, 468–73 (1960).—Refluxing 10 g. *p*-acetaminobenzaldehyde in 130 cc.  $\text{H}_2\text{O}$  with 5 g. NaOH in 20 cc.  $\text{H}_2\text{O}$  30 min., extg. (after cooling and adding  $\text{Na}_2\text{CO}_3$ ) the free aldehyde with Et<sub>2</sub>O, dropping the Et<sub>2</sub>O soln. simultaneously with 4.5 g. NaNO<sub>2</sub> into 300 g. ice and 20 cc. HCl, decanting the Et<sub>2</sub>O layer, filtering the soln. of the diazo compd., removing excess HNO<sub>2</sub> with urea, dropping into a soln. of 10 g. K ethylxanthate and 3 g. K<sub>2</sub>CO<sub>3</sub>, filtering off the ppt. of diazonium ethylxanthate, keeping overnight (loss of N and formation of an oil), extg. with Et<sub>2</sub>O, washing the ext. with an alk. soln. and  $\text{H}_2\text{O}$ , drying, and evapg. *in vacuo* gave *p*-formylphenyl xanthate. Refluxing it in dil. EtOH contg. 6.5 g. KOH 5–6 hrs., removing the EtOH *in vacuo*, dissolving in  $\text{H}_2\text{O}$ , filtering, and adding K<sub>3</sub>Fe(CN)<sub>6</sub> pptd. *p,p'*-diformyldiphenyl disulfide, m.  $108^\circ$  (EtOH). Dissolving this sulfide at the b.p. in a concd. Na<sub>2</sub>S soln. and cooling to  $0^\circ$  gave 50–5% Na salt of *p*-mercaptobenzaldehyde (I). Neutralizing 5 g. ClCH<sub>2</sub>CO<sub>2</sub>H in 10 cc.  $\text{H}_2\text{O}$  exactly with Na<sub>2</sub>CO<sub>3</sub>, adding a few drops *N* NaOH and 6 g. I in  $\text{H}_2\text{O}$ , keeping the mixt. 1 hr. at  $50-60^\circ$ , cooling, adding  $\text{H}_2\text{O}$  if a ppt. formed, acidifying with HCl, filtering off the ppt., dissolving in Na<sub>2</sub>CO<sub>3</sub> soln., pptg. with acid, and washing gave RSC<sub>6</sub>H<sub>4</sub>CHO [R = CH<sub>2</sub>:CO<sub>2</sub>H (II), m.  $177^\circ$ ]. Also prepd. by this method were acid with R = CHMeCO<sub>2</sub>H (III), m.  $101^\circ$ , CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H (IV), m.  $105^\circ$ , CH<sub>2</sub>EtCO<sub>2</sub>H (V), oily, CMe<sub>2</sub>CO<sub>2</sub>H (VI), oily, and CH(CHMe<sub>2</sub>)CO<sub>2</sub>H (VII), oily. The 1st 3 acids were also obtained initially as oils. By repeating the extn. with Et<sub>2</sub>O, dissolving in Na<sub>2</sub>CO<sub>3</sub>, and reprecip. with acid they were purified. Refluxing 4 g. I in 50 cc. 50% EtOH with 3.3 g. ClCH<sub>2</sub>CO<sub>2</sub>Et (for analogs Br compd. used) until the soln. showed neutral reaction, evapg. the EtOH, extg. with Et<sub>2</sub>O, evapg., and distg. *in vacuo* gave analog with R = CH<sub>2</sub>CO<sub>2</sub>Et (VIII), b<sub>1</sub>  $146-9^\circ$ . Also prepd. were esters with R = CHMeCO<sub>2</sub>Et (IX), b<sub>1</sub>  $135-8^\circ$ , CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et (X), b<sub>1</sub>  $165-8^\circ$ , CH<sub>2</sub>EtCO<sub>2</sub>Et (XI), b<sub>1</sub>  $150-3^\circ$ , CMe<sub>2</sub>CO<sub>2</sub>Et (XII), b<sub>1</sub>  $144-8^\circ$ , CH(CHMe<sub>2</sub>)CO<sub>2</sub>Et (XIII), b<sub>1</sub>  $170-2^\circ$ . The thiosemicarbazones were prepd. by mixing at the b.p. the aldehyde acid in 20% AcOH with 10% semicarbazide soln. in slight excess, cooling, and crystg. from 40% EtOH or dil. AcOH. This gave semicarbazones with II, m.  $205^\circ$ , III, m.  $197^\circ$ , IV, m.  $209^\circ$ , V, m.  $182^\circ$ , VI, m.  $219^\circ$ , VII, m.  $183^\circ$ , VIII, m.  $103^\circ$ , IX, m.  $147^\circ$ , X, m.  $121^\circ$ , XI, m.  $124^\circ$ , XII, m.  $107^\circ$ , and XIII, m.  $94^\circ$ . XI showed the highest general antibiotic activity at concns. of 20  $\gamma$ /cc. against *Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, against the fungi *Candida albicans* and *Trichophyton mentagrophytes* and against *Mycobacterium tuberculosis*. VIII and XII were more selectively active against the last organism at 5  $\gamma$ /cc. and XIII at 2  $\gamma$ /cc. II. Thiosemicarbazones of  $\alpha$ -(*p*-formylphenylsulfonyl) acids and esters. *Ibid.* 474–82. —Heating an intimate mixt. of 122 g. *p*-sulfamidobenzoic acid and 257 g. PCl<sub>5</sub> at  $110^\circ$  until the mass lost 150 g. wt., then heating *in vacuo* in an oil bath at  $250^\circ$  while collecting the material distg., pouring the fused distillate into ice, keeping 5–6 hrs., filtering, and drying gave 60–5% *p*-cyanobenzenesulfonyl chloride, m.  $111-12^\circ$ . The corresponding *p*-cyanobenzenesulfonic acid was prepd. according to Fuller, *et al.* (CA 40, 1807\*). NCC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>R were prepd. by refluxing the acid in a small amt. of  $\text{H}_2\text{O}$  with 1 mole halogen ester and EtOH 24 hrs. ( $\beta$ -bromopropionic ester required 40 hrs.), distg. the EtOH and unreacted ester, cooling, extg. with Et<sub>2</sub>O, evapg., and crystg. from petr. ether or CCl<sub>4</sub> and finally from dil. AcOH. This gave the following esters: R = CH<sub>2</sub>CO<sub>2</sub>Et (I), m.  $69^\circ$ , CHMeCO<sub>2</sub>Et (II), m.  $78^\circ$ , CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et (III), m.  $85^\circ$ , CH<sub>2</sub>EtCO<sub>2</sub>Et (IV), m.  $66^\circ$ , CMe<sub>2</sub>CO<sub>2</sub>Et (V), m.  $76^\circ$ . Treating 7.5 g. anhyd. SnCl<sub>4</sub> in 45–50 cc. Et<sub>2</sub>O 3 hrs. with HCl gas, adding 6.5 g. I ester, stirring 4–5 hrs. with HCl passing slowly through the mixt., keeping overnight, decanting the upper layers of Et<sub>2</sub>O-CHCl<sub>3</sub> from the solid (in case of analogs it was an oil), removing the HCl by keeping *in vacuo*, dissolving in  $\text{H}_2\text{O}$ , heating 15–20 min. at  $25-35^\circ$ , cooling, extg. with Et<sub>2</sub>O, drying with CaCl<sub>2</sub>, distg. the solvent, and crystg. from petr. ether or CCl<sub>4</sub> gave OHCC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>R (R = I), m.  $54^\circ$  (dil.

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